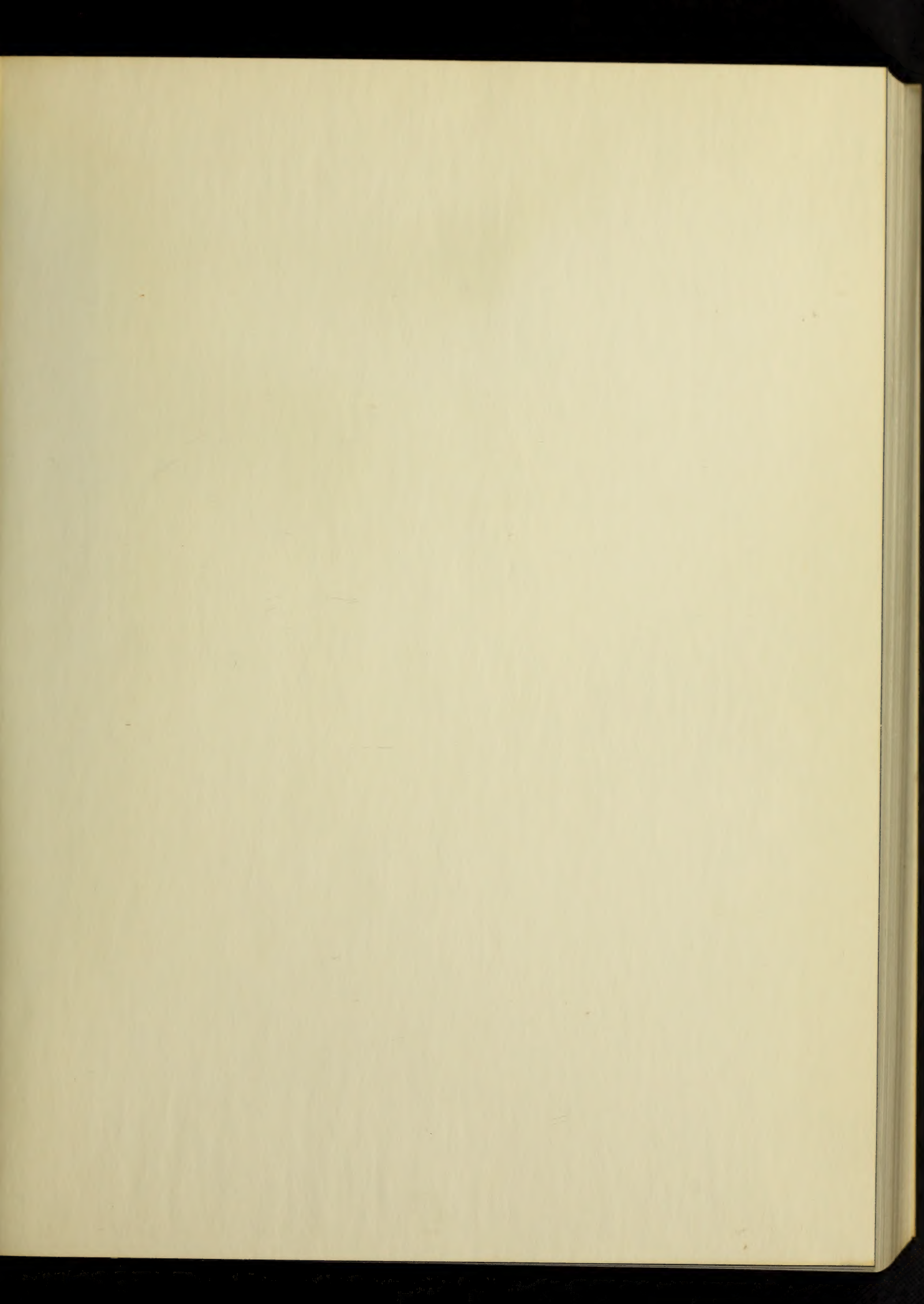
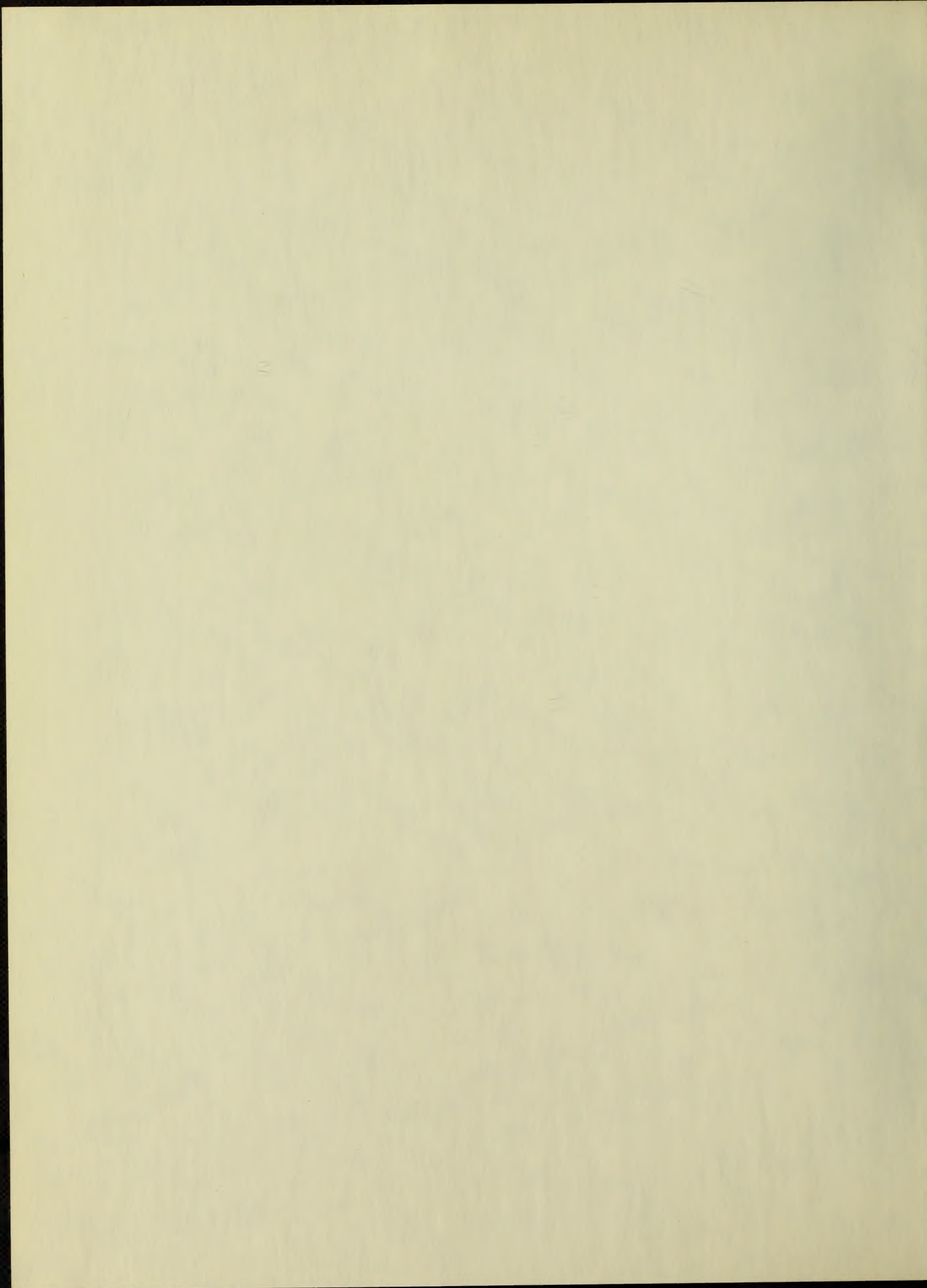
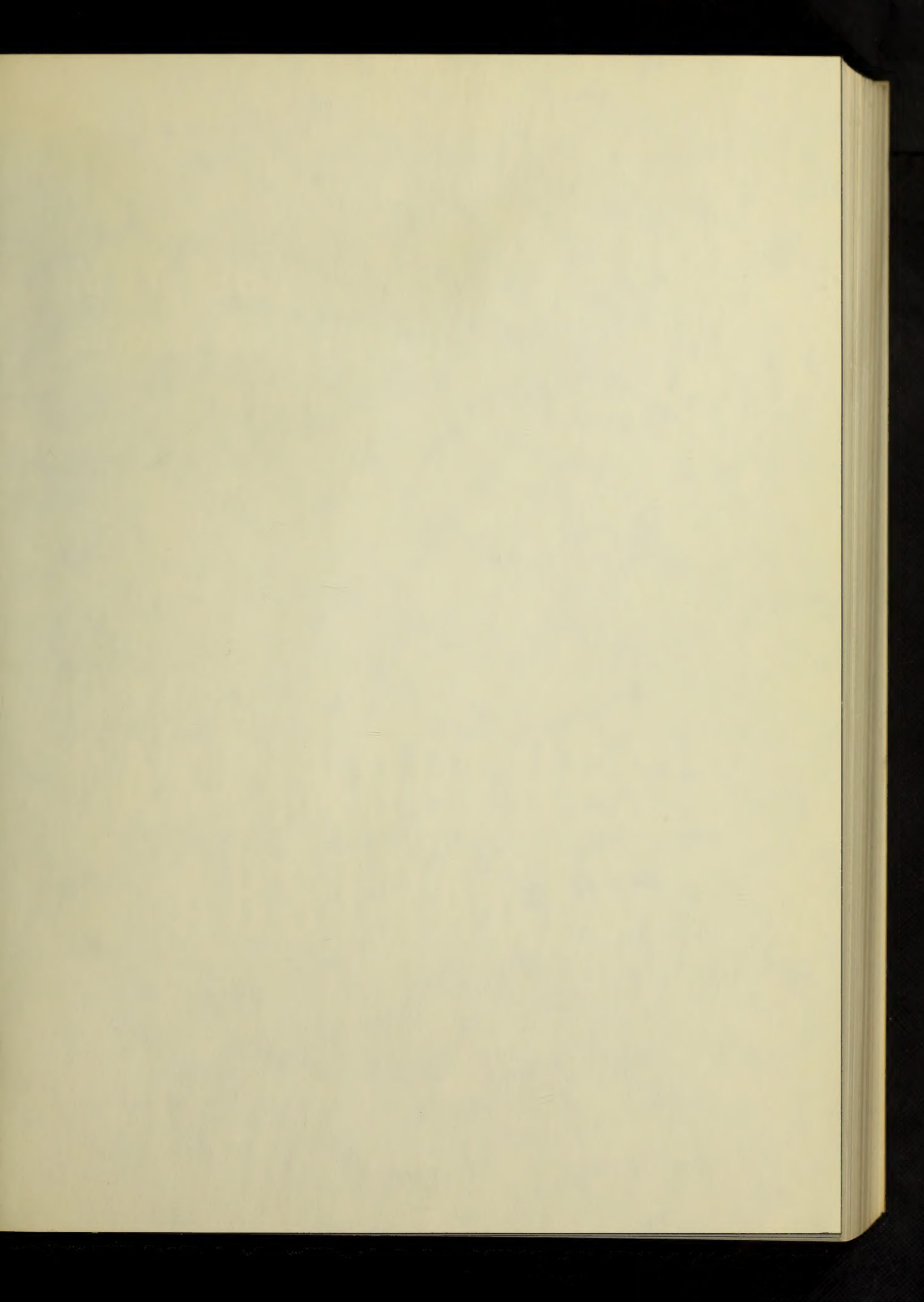


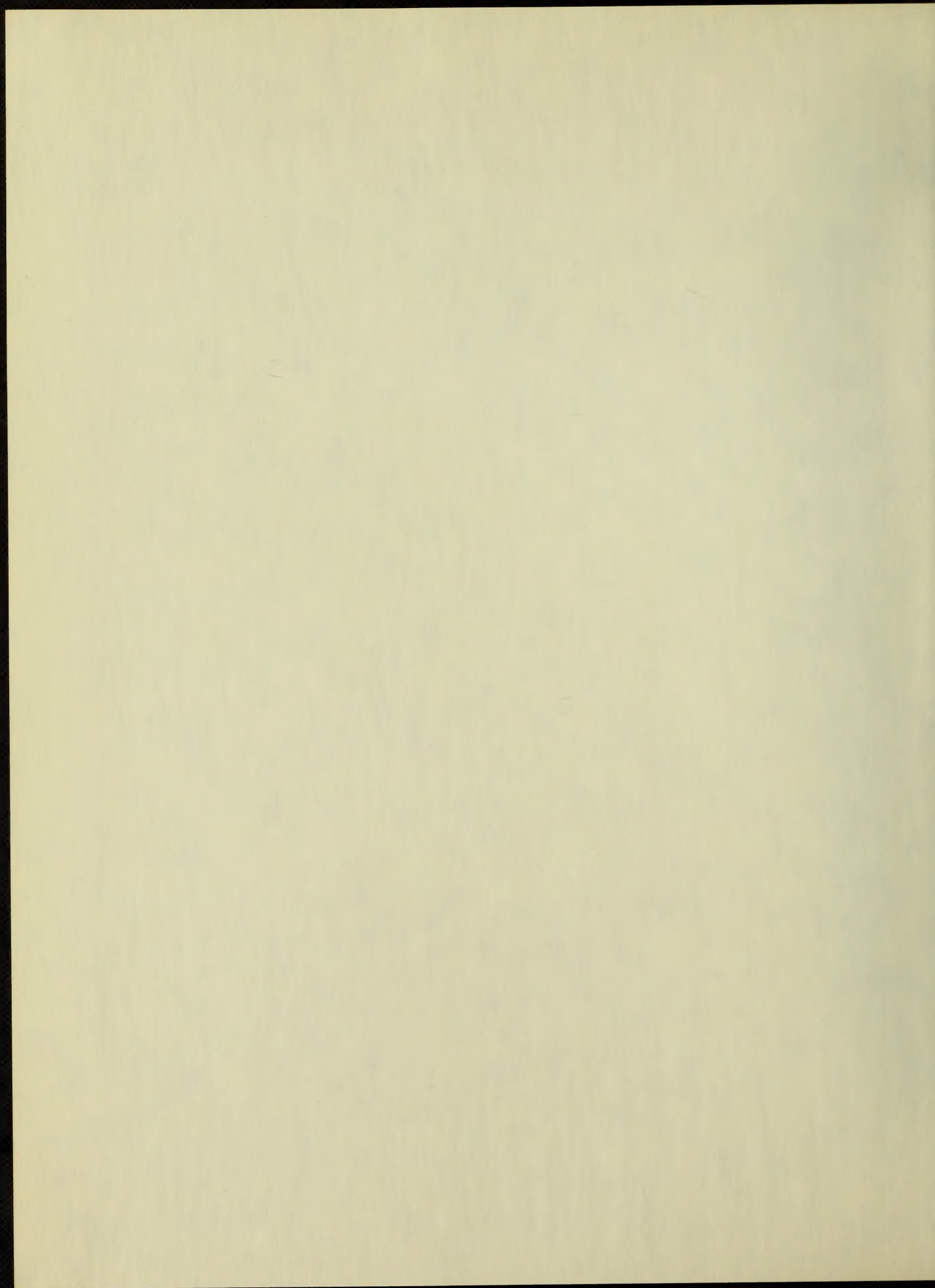
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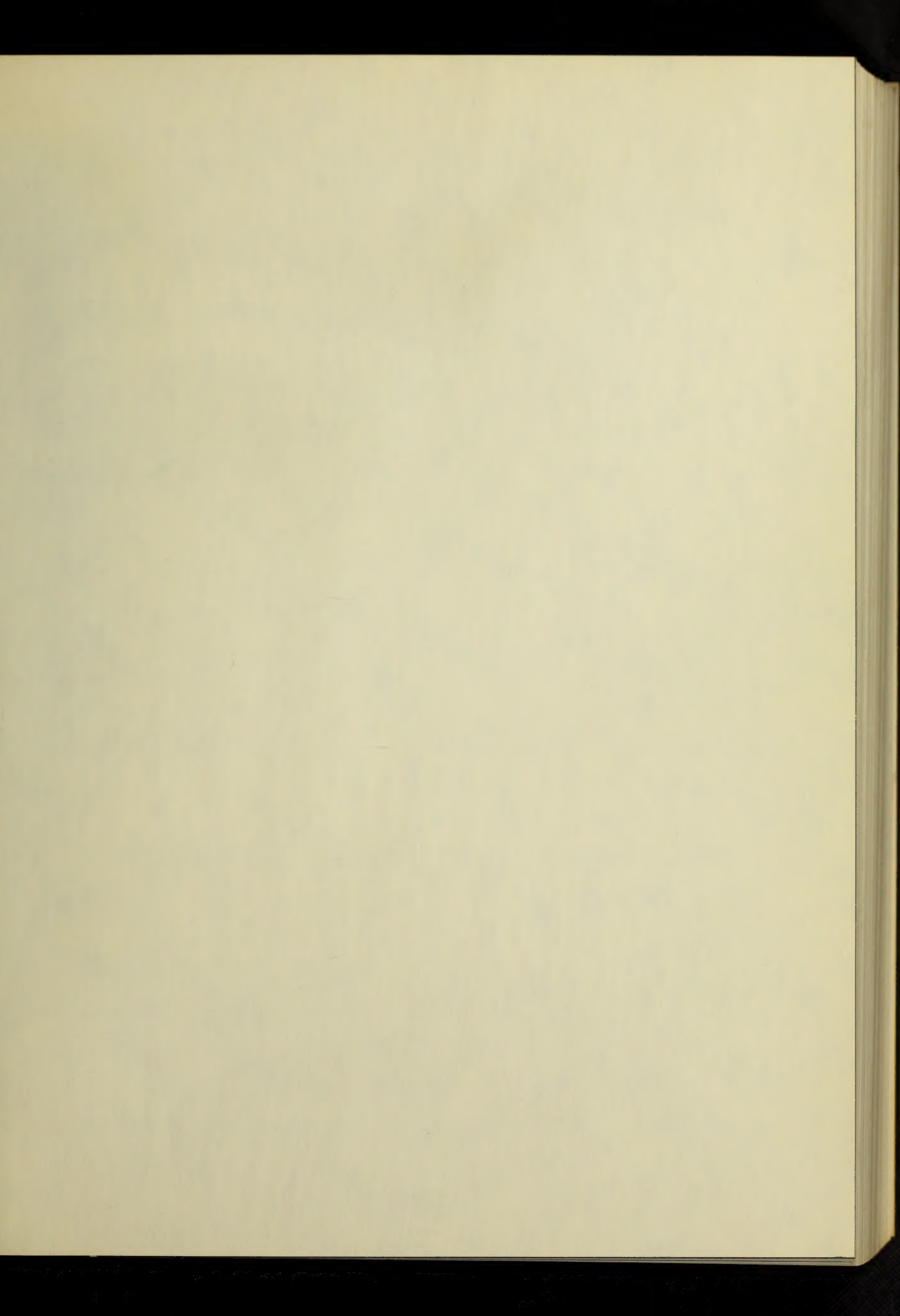
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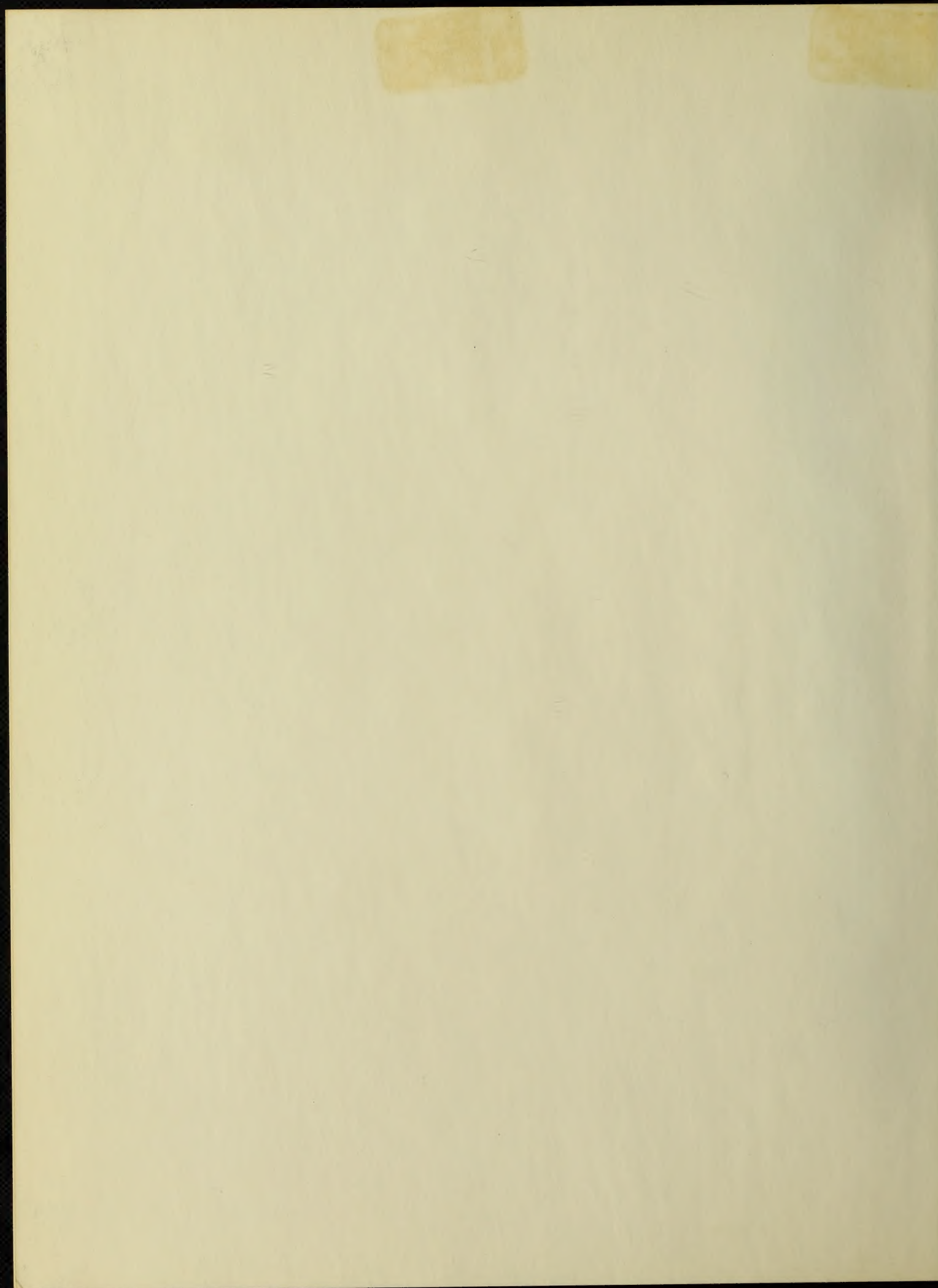






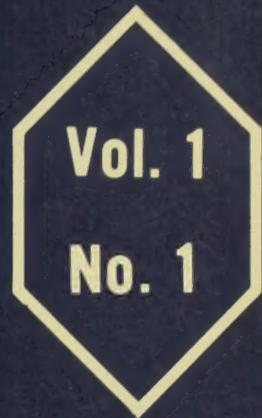






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CARCINOGENESIS ABSTRACTS

National Cancer Institute

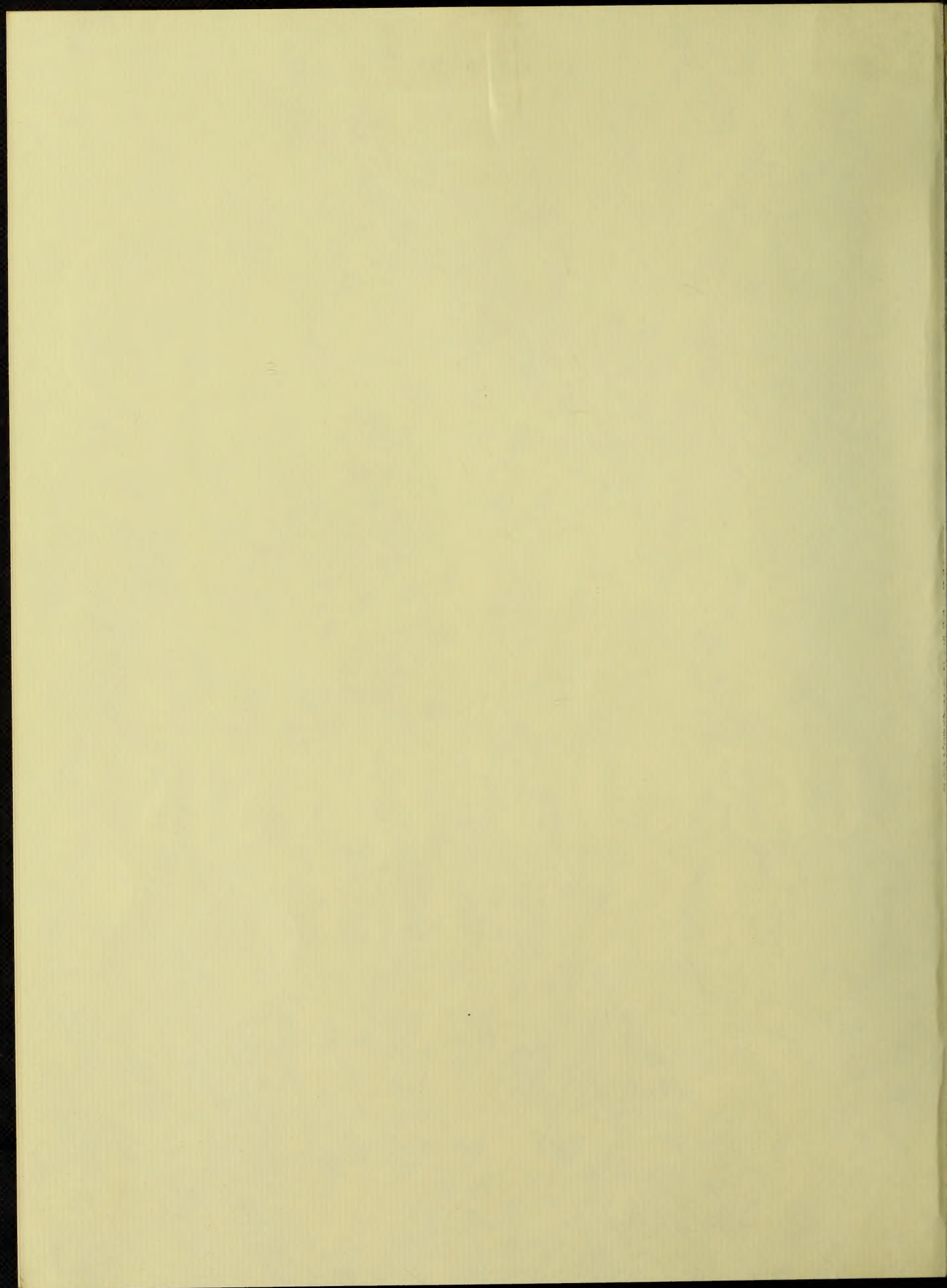
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CARCINOGENESIS ABSTRACTS

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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Bethesda 14, Maryland

63-1 INFLUENCE OF HOST FACTORS ON THE GROWTH OF NEOPLASTIC CELLS. (E.) Furth, J. (Columbia U., New York). Cancer Res. 23(1): 21-34, 1963.

This review surveys present knowledge and assesses current theories on the role of the host in the initiation and promotion of neoplastic disease. It deals in some detail with hormones in the restraint and promotion of neoplasia; with cancer immunology, stressing quantitative autochthonous immunity studies; with viral tumors, their immunologic and hormonal aspects; and with homeostatic mechanisms, giving schematic operational charts for various endocrine functional interrelationships. Considered more briefly are: recent findings in plant tumors; nutrition and antimetabolites; contact inhibition of growth; tumor formation from misplaced normal cells; the resistance of specific organs; and age in growth regulation. (97 references)

63-2 BACTERIOLOGICAL APPROACHES TO CANCER RESEARCH. (E.) Wynne, E. S. (M. D. Anderson Hosp., Houston, Texas) and L. A. Irvine. Texas Rep. Biol. Med. 20(4):532-544, 1962.

Citing prior work on stimulation by carcinogens of the spores of mesophilic Clostridia at 75°, the authors feel further investigation of suitable bacteriological screening technics for carcinogens is warranted. Studies with bacterial models involving competitive substitution for strong carcinogens by less carcinogenic compounds offer a promising approach to questions relative to carcinogenic mechanisms. Also reviewed are bacterial systems of use in the diagnosis of cancer and as part of a screening procedure for uncovering cancer chemotherapeutic agents. (68 references)

63-3 THE COMPLEX PATHOGENIC EFFECT OF TUMORS. (E.) Sinkovics, J. G. (M. D. Anderson Hosp., Houston, Texas), C. C. Shullenberger and C. D. Howe. Exp. Med. Surg. 20(4):277-298, 1962.

In this review of the complexity of laboratory oncogenesis nonspecific modifying factors discussed include hemagglutinins, tumor antigens, antibodies, inhibitors, interferon, lymphoid cells with antitumor activity, passenger viruses, and toxicity. The protean changes in behavior of some animal viruses are considered. While a specific oncogenic virus may be considered as the principal etiologic agent in certain forms of laboratory and natural tumors, no reliable or reproducible data are as yet available to support the existence of human carcinogenic or leukemogenic viruses. However, circumstantial evidence appears to indicate that such agents exist. Some human leukemia tissue cultures contain electron microscopically demonstrable virus particles, but material from such cultures has not, thus far

induced neoplastic disease in inoculated laboratory animals. If human oncogenic viruses exist, some factors in their isolation and maintenance are not yet understood. The effects of cell fractions and nucleic acids on tumor initiation and growth are briefly mentioned. (135 references)

63-4 SKIN CANCER AND SUNLIGHT. (E.) Howell, J. B. (U. Texas Southwestern Med. Sch., Dallas, Texas). Skin 1(6):197-199, 1962.

In a general summary of the converging evidence involving sunlight as the major cause of skin cancer, etiologic factors considered are: geographic location (regions of high insolation), skin pigmentation (fair), residence and occupation (rural, outdoor); all are factors affecting the pattern of incidence of solar skin damage in man. Sunlight first produces damage to the subpapillary vascular plexuses, then degeneration of collagen, which in turn exerts profound effects on the overlying epidermis. It is this degenerated ("Sailors", "Farmer's", or "Solar") skin which produces solar keratoses, the solar type of leukoplakia, squamous cell carcinoma, and some basal cell cancers. (19 references)

63-5 THE INDUCTION OF TUMORS AND ENZYMES. (E.) Boyland, E. (Dept. Biochem., U. London, England). Pp. 135-140 in On Cancer and Hormones: Essays in Experimental Biology. Chicago, U. Chicago Press, 1962. \$8.50.

In a discussion of the variations in latency period among different carcinogens, some early, rapid effects of delayed tumor induction are considered. Such are the stimulation, by carcinogenic hydrocarbons, of the activity of liver microsomal enzymes, and of the synthesis and excretion of ascorbic acid. Protein production appears to be involved in the former, and growth inhibition by carcinogenic hydrocarbons may be due to the preferential use of proteins for enzyme synthesis rather than for growth. Cancer cells may be cells in which the normal suppressors or controls over enzyme activity and growth and division are deficient or altered. The problem of the long delay normally associated with carcinogenesis remains unanswered. (21 references)

63-6 DEVELOPMENTAL STAGES OF MOUSE SQUAMOUS CELL CARCINOMA: AUTORADIOGRAPHIC INVESTIGATIONS USING H³-THYMIDINE, H³-CYTIDINE, AND H³-LEUCINE. (E.) Oehlert, W. (Inst. Path., U. Freiburg, Germany) and J. Côté. Pp. 541-552 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

During the transformation to malignancy, the distribution and incorporation of tritium-labeled thymidine, cytidine, and leucine or uridine in cells of mouse epidermis painted with 20-methyl-

cholanthrene (in benzene) showed: (1) increased incorporation of leucine into the protein of nucleus and cytoplasm on the 2nd day; (2) constant increase in protein synthesis until carcinoma development; (3) increased nuclear RNA synthesis within 60 min.; in fully developed carcinoma, there was a more rapid transfer of such RNA to the cytoplasm and also disproportionately greater increase of RNA synthesis in relation to the size of the nucleus; (4) increased DNA-synthesizing cells in the basal layer on the day 2, and again at time of papilloma formation; (5) formation, in the reticulizing zones, of a new cell type--small, spindle-shaped, permanently undifferentiated and capable of DNA synthesis indefinitely. These histoautoradiographic data indicate that the transformation of epidermal cells to malignancy occurs by the collapse of the normal physiologic regulatory mechanism of cell growth, whereby after each division one daughter cell becomes differentiated while the other remains embryonic and undifferentiated. The carcinogen, by altering the cytoplasmic proteins, speeds up DNA synthesis and interrupts its rhythmic inhibition; endomitosis, amitosis, and mitosis follow, with the loss of tissue and organ specificity, and in the fully developed carcinoma only a single cell type is produced, an undifferentiated embryonic type, capable of further division.

- 63-7 PRECANCEROUS LESIONS IN CHEMICAL CARCINOGENESIS. (E.) Khanolkar, V. R. (Indian Cancer Res. Ctr., Parel, Bombay, India). Pp. 53-54 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Briefly reported is work in 3 areas of research. Among sulfur analogs of carcinogenic hydrocarbons synthesized and tested for carcinogenicity to evaluate the role of the K- and L-regions, a few initiated lesions which, however, failed to develop into palpable tumors. A test of the extracts of sun-cured tobacco leaves in various solvents failed to identify a positive carcinogenic fraction. An alkaloid-containing whole extract induced massive hyperplasia of the epidermis. This extract, made alkaloid-free, induced frank carcinomas with the addition of croton oil. Elaborate studies have been carried out on the induction of mammary cancer by 20-methylcholanthrene and 1,2,5,6-dibenzanthracene in 5 strains of mice. With strain A mice, results were negative, a failure attributed to a lack of adequate effect of the hormonal factor--the promoting agent in mammary carcinogenesis. These studies point out the importance of promoting agents in carcinogenesis. (5 references)

- 63-8 HORMONES AS INDUCERS OF THE MORPHOLOGICAL PRECURSORS OF CANCER. (E.) Mühlbock, O. (Netherlands Cancer Inst., Amsterdam, The Netherlands). Pp. 9-20 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Drawing on experimental work chiefly in regard to hormone dependent tumors of the breast, uterus, ovary, and pituitary, this review stresses the fact that while there are many differences in the pathway of the development of these tumors, one common feature is apparent: the "borderland" between normal and malignant growth is broad, and the changes from normal via hyperplasia to benign tumors and to malignant new growth can be more readily studied. The study of endocrine tumors makes it clear that a malignant tumor is not in a definite state from the onset and does not remain unchangeable. Thus, endocrine tumors offer a valuable tool for the exploration of the processes of development and differentiation. (13 references)

- 63-9 THE CHEMICAL BASIS OF CARCINOGENESIS. (E.) Haddow, A. (Chester Beatty Res. Inst., London, England). Pp. 1-7 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

One remarkable feature of the carcinogenic process, as seen experimentally, is the great number and variety of agents--chemical, physical and viral--which may set it in motion. While much has been learned about the chemical constitution and biological action of various families of hydrocarbons, the possible mode of action was left undefined, except as regards dependence upon some special kind of chemical reactivity. The biological activity of some compounds appears to be related to substitutions at the phenanthrene bond and which may be related to a certain electron density in the so-called K-region, however, other active compounds lack this feature. In the case of alkylating carcinogens, the situation is more amenable, no doubt because of their higher reactivity, their comparative molecular simplicity, and their possession of features strongly suggestive, or perhaps even indicative of possible modes of action. In the past, it has often been assumed that chemical carcinogens might, in certain situations, operate by the unmasking of latent viruses already present. For such a view there is little real evidence. On the other hand, the undoubted importance of nucleic acids in many viral structures, and the question of the possible infectivity of such nucleic acids in themselves, raises the alternative question: whether the transformation induced by the viruses relatively specifically and often speedily, may not be similar to, or identical with, that evoked by chemical agents rather less specifically and over necessarily longer periods of time. (8 references)

- 63-10 PANEL DISCUSSION: THE RELATION BETWEEN TOBACCO SMOKE AND CANCER OF THE LUNG. (E.) Haddow, A., Moderator (London, England). Pp. 655-666 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

L. M. Shabad indicated results in the experimental

production of tumor from substances in tobacco smoke were at first paradoxical. He definitely implicated 3,4-benzpyrene as the active carcinogenic agent of tobacco tar. Only recently has success been attained in the production of experimental epidermoid lung cancer in rats by intratracheal insufflation of large doses of carcinogenic hydrocarbons. W. H. Carnes reported that while no atypical metaplasia and no carcinoma in situ were found in over 2000 autopsy cases from 5 cities, there was an increase in all other types of metaplasia (transitional, squamous, regenerating) among those considered heavy cigarette smokers. L. Kreyberg, showed an increase in the ratio of epidermoid (and small cell anaplastic) carcinoma versus adenocarcinomas (and carcinoids) was related to the amount of tobacco smoked per day (in a group of Norway males, ratio for non-smokers was 0.3:1; for those who smoked 4, 19, or 19 g/day, ratios were 0.5:1, 3.8:1, and 8.3:1, resp. P. R. Peacock reported his mice and other animals were "smoking", taking in the smoke through the mouth. He felt it was a delusion to consider 3,4-benzpyrene "and such things" in smoke as a cause of lung cancer in man. G. J. Cunningham (the only cigarette smoker on the panel) stated that the increase in lung cancer (which he questioned) would have to be of the squamous cell variety; he would remain in doubt until someone could produce not only experimental tumors of the lung, but squamous cell carcinoma of the lung.

63-11 ON THE CONNECTION BETWEEN SMOKING AND BLADDER TUMOURS. (E.) Clemmesen, J. (Dept. Path., Finsen Inst., Copenhagen, Denmark). Pp. 451-462 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

A study based on interviews was made of the use of tobacco by male pts. in Copenhagen who had bladder tumors and a group of matched controls; some comparisons were also made to the general population of Denmark. There appears to be a real increase in the incidence of bladder tumors, particularly among men in Copenhagen, where rates rose from 8.0/100,000 in 1943 to 28.1 in 1957. There is a tendency, which is statistically significant, for pts. to smoke more cigarettes than controls, and among older pts. to smoke more cigars. In terms of total tobacco consumption per day, more controls and normal population used 6-15 g/day than pts.; at 16-25 g/day, all 3 groups were about equal while the frequency among those consuming more than 26 g/day was highest for the tumor pts. by a factor of about 3. The association between bladder tumors and tobacco smoking is less pronounced than between bronchial carcinoma and cigarette smoking. Since bladder tumors occur also among nonsmokers, other carcinogenic factors also play some part. The author feels justified in dissuading pts. from continuous smoking of cigarettes or cigars once they have developed a papilloma of the urinary bladder. (13 references)

63-12 PATHOGENESIS OF OVARIAN TUMORS IN MICE TREATED WITH CHEMICAL CARCINOGENS. (E.). Marchant, J. (Cancer Res. Lab., Dept. Path., U. Birmingham, England). Pp. 709-715 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In a summary of recent findings, it is reported that preneoplastic changes induced by skin painting with dimethylbenzanthracene (DMBA) consisted, in all treated mice, of progressive ovarian atrophy, with gradual disappearance of follicles and of almost all oocytes. The few corpora lutea which remained became fused into masses; the lutein cells became vacuolated and pigmented or hyalinized. When all follicles had disappeared, neoplastic changes set in, with the appearance of nodules of granulosa-celled tumor. Non-tumorous ovaries atrophied further, showing premature senility. Preneoplastic ovaries from DMBA-treated mice, bilaterally transplanted to untreated oophorectomized hosts, proceeded to form tumors even when transferred only 10 days after a single treatment; but untreated transplanted ovaries formed none. After unilateral ovary exchange, presence of a normal ovary inhibited tumor development, as did hypophysectomy.

63-13 PROPERTIES OF CELLS TRANSFORMED BY POLYOMA VIRUS. (E.) Vogt, M. (Div. Biol., Calif. Inst. Tech., Pasadena) and R. Dulbecco. Pp. 367-374 in Basic Mechanisms in Animal Virus Biology. V. 27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

In a general discussion and review of their own work on the mechanism of action of tumor-producing viruses, the authors provide a detailed comparison of the characteristics of "early" and "late" transformed cells from hamster embryo cultures, infected with polyoma virus and developed in cultures with low or high cell concentrations, resp. The physiological properties of late transformed cells are described with respect to morphology, culture pattern, rate of growth, maximum cell density at saturation, tumor production in hamsters, efficiency of cloning, resistance to heterologous antibody and their relationship to polyoma virus. The results showed that these cells are highly atypical, due probably to changes in the cell surface; viral DNA can no longer be isolated from them. The efficiency of cloning, morphology of clones formed, transplantability into 20-day old hamsters and the presence of polyoma virus were then investigated in the early transformed cells; again, no virus could be detected. Multilayered clones were produced, and a high proportion of the cells showed aneuploid chromosome numbers and chromosome bridges. The late transformed cells are tentatively interpreted as derived from the early transformed cells by a secondary variational process. (7 references)

- 63-14 THE CYTOLOGY OF ROUS SARCOMA VIRUS INFECTION. (E.) Vogt, P. K. (Virus Lab., U. Calif., Berkeley) and H. Rubin. Pp. 395-405 in Basic Mechanisms in Animal Virus Biology. V. 27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

In an extensive review of both the literature and their own work on the cytopathic changes occurring in chick embryo cells following infection with Rous sarcoma virus (RSV), the authors emphasize the RSV-induced changes at the cell surface. The localization of RSV antigen in infected chick embryo cells is reviewed and described on the basis of a chick embryo culture infected with an average of 1 focus-forming unit of RSV/cell. Particular attention is given to the use of dark-field microscopy for studies on the morphology of the cell surface, as well as the use of electron microscopy to study virus formation. Finally, a direct comparison is made between antigenic sites and particle aggregates at the surface of Rous sarcoma cells, and the cytological findings are correlated with the growth and localization of infectious RSV. The results indicate that completion of RSV occurs at the cell membrane. (33 references)

- 63-15 BENIGN LESIONS AND CANCER OF URINARY BLADDER. (E.) Raso, M. (Inst. Morbid Anat., U. Padua, Italy). Pp. 441-449 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

A discussion of the etiology and pathogenesis of benign and malignant bladder neoplasms, based on personal examination of about 1000 bladder tumor biopsies. The histological diagnosis and classification of papillomas is considered in some detail, with special reference to the prognosis in recurrent lesions. Hyperplasia and metaplasia in bladder tumors, as related to leukoplakia, cystitis, and exstrophy are also examined, as well as the importance of ectasiae in tumor formation. It is concluded that hyperplastic and metaplastic alterations of the vesical epithelium are often the first stages in neoplasia. Various nonspecific irritative factors, and malformations, are important as elements determining the morphological variety of the tumor (pseudoglandular, squamous, etc.), rather than as etiological factors.

- 63-16 CANCER EPIDEMIOLOGY--IMPLICATIONS FOR CONTROL. (E.) Breslow, L. (State Dept. Pub. Health, Berkeley, Calif.). Am. J. Public Health 53(2):218-222, 1963.

The role of the epidemiologist in present-day cancer control is discussed, stressing research on causative factors which will permit primary prevention; forwarding measures designed to find and treat cases early; and to serve as a collaborative research tool with other relevant

sciences such as virology in elucidating the natural history of the disease.

- 63-17 NERVOUS STIMULI AND TUMORIGENESIS. (E.) Lipschutz, A. (U. Santiago Fac. Med., Chile). Pp. 205-212 in On Cancer and Hormones: Essays in Experimental Biology. Chicago, U. Chicago Press, 1962. \$8.50.

In a general survey of the role of nerve stimuli in carcinogenesis and tumor inhibition, the author deals briefly with findings which include: the maintenance of steroid homeostasis through the hypothalamic-hypophyseal mechanism; the significant incidence of cervical cancer in certain psychic maladjustments; the enhancement, by physiologic stress or induced "neuroses", of hormone-dependent tumors, and its abolition by bromides; the role of tranquilizers in hastening tumor development in susceptible subjects; the induction, by nerve section, of gastric cancer in a giant species of Orthoptera; the local, unilateral "protective" suckling effect in tumor inhibition. All are mentioned as actual or potential factors in the initiation or promotion of cancer and in its inhibition or therapy. (35 references)

- 63-18 ONCOLOGY AND GERONTOLOGY: GENETIC IMPLICATIONS. (E.) Strong, L. C. (Roswell Park Mem. Inst., Springville, N. Y.) and F. Johnson. Pp. 119-151 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Distribution in terms of longevity, incidence and latency of spontaneous tumors was studied in the descents of 6 sublines of F₁ Brpd/St x C57/St mice (maintained by sister-brother matings) established in the following maternal age classes (days): I, < 100; II, 101-200; III, 201-300; IV, 301-400; V, 401-500; VI, 501-600. Percentage incidence of total tumors did not vary between maternal classes II-V (32.8, 33.9, 33.5 and 34.5, resp.). In class I, deviation was shown by females because of a high incidence of mammary carcinoma (70%); at the other extreme in class VI, males exhibited a deviation above the approximately 34% level, while females deviated below. The high incidence of mammary carcinoma in class I females was reduced to 0 in class VI (although there were only a few individuals available); other types of tumors, particularly leukemia, replaced the mammary tumors in the later maternal classes. There was a gradual increase in life expectancy (for all mice) beginning in class I (628 days), reaching a maximum in class III (681 days), with decline in class V to 666 days; average longevity was greater for males, but this was influenced largely by the high early mortality of females in offspring of class I. Class I males developed tumor 22.6 days after the average life span of the non-tumor class of the same descent. In classes II and IV, average age of onset of tumors was 57.3 and 57.1 days difference, resp., after the average longevity of non-tumor bearing

males of the same maternal age descent. It appears that the males in order to give rise to a tumor must live beyond the life span of the males that die without tumors. Genetic and environmental interpretations of the findings are discussed.

- 63-19 ON THE PROGNOSIS OF PRECANCEROUS CONDITIONS OF THE UTERINE CERVIX. (E.) Clemmesen, J. (Radium Hosp., Copenhagen, Denmark). Pp. 463-466 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Two series of cases were reviewed to determine the prognosis in pts. with precancerous conditions of the uterine cervix: the study of O. Petersen (1955) whose pts. were seen at the Radium Hospital; and P. Lange (1960) whose pts. came from a Municipal out-patient clinic. In Petersen's study, among 327 pts. with simple epithelial hyperplasia, 1 developed carcinoma after 5.6 yr.; of those with epithelial hyperplasia + nuclear abnormalities, 20/84 (24%) developed carcinoma in 15 yr.; where there was suspicion of invasion, 14/43 (33%) developed carcinoma in 8 yr. In P. Lange's series, 18/83 (22%) who showed epithelial hyperplasia + nuclear abnormality developed carcinoma in 5 yr.; where there was suspicion of invasion, 6/17 (35%) developed carcinoma in 5 yr.

- 63-20 MECHANISMS OF CARCINOGENESIS. (E.) Arley, N. (Norwegian Radium Hosp., Oslo, Norway) and R. Eker. Advances Biol. Med. Phys. 8:375-436, 1962.

After pointing out the limitations of our knowledge with respect to the difference between normal and malignant cells, as well as some of the unsolved problems relating to the reproduction of both normal and pathological tissue, the authors review some of the basic experimental findings underlying the currently propounded theories of carcinogenesis. Following a discussion of mathematical models of carcinogenesis, the authors apply mathematical technics to the analysis of experimental results with tumor induction by chemical agents, viruses, ultraviolet radiation and radioisotopes and ionizing radiation. The authors conclude that a fair qualitative and quantitative description of all the experimental findings on carcinogenesis, by whatever agent, can be provided by a stochastic model which assumes that neoplasia can be initiated by a single energy transfer directly from the carcinogen to the DNA molecules of the genetic apparatus of the somatic cells. In some cases, however, indirect energy transfers, such as via intermediary free radicals or other secondary reaction products, may play a role in carcinogenesis. In the case of radiation carcinogenesis the model leads to a single but sufficiently flexible dose-response relationship without, but in some cases simulating, a threshold dose, which can be fitted with good agreement to data showing

a linear or sigmoid form, and a form with a maximum. Future experimental investigations are suggested by the use of the model for guidance. (172 references)

- 63-21 ANTIGENIC PROPERTIES OF CELLS TRANSFORMED BY POLYOMA VIRUS. (E.) Habel, K. (NIH, Bethesda). Pp. 433-439 in Basic Mechanisms in Animal Virus Biology. V.27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn. 1962.

In a general discussion of his previously published work on the susceptibility of mice and hamsters to transplantable tumors, particularly those originally induced by polyoma virus, the author reviews the *in vivo* and *in vitro* evidence for the presence of a new antigen in cells transformed by polyoma virus and the relationship between this antigen and the virus itself. *In vivo* evidence cited includes the increased susceptibility to polyoma tumors in immunologically immature or X-irradiated animals, the resistance of virus-immune adults to challenge with polyoma tumor, immunization with tumor cells against tumor challenge, the increased susceptibility of adult mice to tumor challenge after inoculation with tumor cell antigen at birth, and enhanced resistance after repeated challenge with tumor. Evidence is also cited for the presence of polyoma tumor antigen in hamster or mouse embryo cultures transformed *in vitro*. However, since the transformed cells contain no demonstrable virus, the tumor antigen must be cellular rather than viral in origin, and the information necessary for its production must be transmitted genetically to the daughter cells. The existence of such a "foreign" cellular antigen in transformed cells probably explains both the refractoriness of adult animals to oncogenesis by polyoma virus and the resistance of virus-immune adults to transplantation of isologous polyoma tumors.

- 63-22 THE S-E-POLYOMA VIRUS. (It.) Castelli, L. (Higher Inst. Health, Rome) and A. M. Jemolo. Recenti Progr. Med. (Roma) 33(4):286-310, 1962.

In an extensive review of the anglo-american literature, the authors discuss the history of the viral theory of cancer, the isolation of SE polyoma virus from parotid tumors in C3H mice and leukemic AKR mice, the comparative characteristics of polyoma virus and the viruses isolated from various other types of tumors, the pathogenicity of polyoma virus in mice, rats and hamsters, the hemoagglutinating and antigenic properties of polyoma virus, and the relationships between the virus and the host cell (synthesis of virus in sensitized cells and cultivation in various tissues). The authors conclude that the presence of virus is apparently not necessary for the transmission of malignant characteristics to daughter cells following

induction of a neoplastic state by means of a virus. (66 references)

- 63-23 INTERACTION BETWEEN TUMOR VIRUSES AND CELLS IN CYSTS AND TUMORS INDUCED BY THESE VIRUSES IN VARIOUS ANIMAL SPECIES. (E.) Zilber, L. A. (Gamalei Inst. Microbiol. and Epidemiol., Acad. Med. Sci., Moscow, USSR). Pp. 513-517 in Basic Mechanisms in Animal Virus Biology. V.27 in Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

Rous sarcoma virus (RSV) in rats induced (a) cyst formation through destruction of lymphoreticular and vascular endothelial tissue, and (b) at a later date, sarcomas. In rabbits, interaction with RSV led to the development of benign tumors, which were usually resorbed. Cysts in mice could be induced by sheep pulmonary adenoma virus: polyoma virus causes both infectious and neoplastic processes in mice. Cyst formation began with cell proliferation, and cell destruction followed. The interaction which brings about the viral transformation of its host tumor cell may be due to integration into the cell of foreign genetic information from the virus, by mechanisms unknown. Why only an occasional cyst undergoes neoplastic transformation is also still unknown. (17 references)

- 63-24 THE VERTICAL AND HORIZONTAL TRANSMISSION OF AVIAN VISCERAL LYMPHOMATOSIS. (E.) Burmester, B. R. (Agr. Res. Serv., East Lansing, Mich.). Pp. 471-477 in Basic Mechanisms in Animal Virus Biology. V.27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

This review on the transmission of avian lymphomatosis is largely devoted to the work of 2 laboratories. Several different avian leukosis viruses induce resistance to infectious foci (RIF) of Rous sarcoma virus, and all RIF-associated viruses examined can induce visceral avian lymphomatosis, but under usual conditions relatively few infected birds develop overt symptoms. This virus is transmitted congenitally from hen to egg (vertically) and the infected, fertile egg is most important in survival of the virus. Horizontally it is transmitted between chickens of the same hatching or rearing unit, in genetically susceptible strains. Chickens heavily infected as embryos, or shortly after hatching, carry a prolonged, immunologically tolerant infection without detectable antibodies. Similar chickens exposed at several weeks of age, after transient infection, develop antibody. Most infections do not result in tumor formation. (35 references)

- 63-25 THE PRENEOPLASTIC HYPERPLASTIC ALVEOLAR NODULE AS THE MORPHOLOGIC

PRECURSOR OF MAMMARY CANCER IN MICE. (E.) DeOme, K. B. (Dept. Zool., U. Calif., Berkeley), S. Nandi, H. A. Bern, P. Blair and D. Pitelka. Pp. 349-368 in The Morphological Precursors of Cancer. Severi, L. (Ed.) Perugia, Div. Cancer Res., 1962.

A review of current knowledge about preneoplastic hyperplasia of mammary alveolar nodules in mice, and the factors which may affect their change to mammary cancer. These hyperplastic nodules consist of cell populations with altered hormonal requirements and cancer-producing capabilities, which vary within and between each other in growth rate, secretory status, and tumorigenic capacity. The malignant transformation of the nodule is not attributable to latent tumor cells, nor (probably) to somatic mutation, but depends upon the prior occurrence of changes characteristic of nodule cells, such as changes in interaction between the genetic constitution of the host, its hormonal milieu, and mammary tumor virus (MTV) infection. Nodule and tumor formation may be promoted by various hormone combinations, probably somatotrophic hormone (STH) in virgins and mammatropic hormone (MH) in breeding females. Infection with MTV increased responsiveness to STH-containing hormone combinations in some mouse strains (C3H/Crgl or C57Bl/Crgl), to MH-containing combinations in others (A/Crgl). MTV also increased cancer production from nodules; but nodules which are poor cancer producers are not altered by transplantation into MTV-infected hosts. Patterns of MTV interaction with mammary gland tissue, as well as responsiveness to STH-containing hormone combinations, seem to be genetically controlled. The diversity and stability of the cell populations derived from these nodules make them useful in carcinogenesis research. (46 references)

- 63-26 CONTACT-DEPENDENT BEHAVIOR OF NORMAL CELLS AND THE POSSIBLE SIGNIFICANCE OF SURFACE CHANGES IN VIRUS-INDUCED TRANSFORMATION. (E.) Abercrombie, M. (Dept. Zool., U. Coll., London, England). Pp. 427-431 in Basic Problems in Animal Virus Biology. V.27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

In tissue cultures, the ordered monolayer growth of fibroblasts is normally controlled, in part, by the contact inhibition of cell locomotion. This review considers some factors which cause the failure of that morphogenetic control. Cell population density and other environmental variables may increase the amount of cell overlap. Contact inhibition may be greatly reduced, between sarcoma and normal cells, by changes of cell surface properties which inhibit mutual cell adherence and adherence to the substrate. A loss of homologous contact inhibition may produce such multilayering as occurs in cells transformed by polyoma virus. Increased mitosis and increased production of intercellular substances may also produce local multilayers. Cell degeneration, mass migration, and cell fusion are other factors involved in

Issue morphogenesis. Virus may utilize any one or several of these mechanisms in its interference with normal cell behavior. (40 references)

- 3-27 LEUKEMOGENESIS DUE TO RADIATION. (Fr.)
Lacassagne, A. J. Radiol. Electr.
3(12):803-805, 1962.

In a report presented at the 10th International Congress of Radiology in August, 1962, the author reviews the recent literature on the relationships between irradiation and leukemia in both man and mice. The possibility of either a direct or an indirect effect from radiation is discussed, as well as the experimental evidence for the role of a virus in murine leukemia. The author concludes that the various types of leukemias may well differ in etiology, but that genetic factors, chromosomal anomalies and viral agents probably play an important role in all cases, including those induced by irradiation. (23 references)

- 3-28 TOXICITY OF THE "INTENTIONAL" CHEMICAL
FOOD ADDITIVES. I. EMULSIFYING,
SWEETENING AND COLORING AGENTS. (It.) Fecchino, A.
Inerva Farm. 11(11):202-206, 1962.

After pointing out that acute toxicity due to food additives is rare but that these chemicals may well have a cumulative effect on the organism, an indirect injurious effect, or may be toxic to man even though safe for animals, the author lists the principal emulsifying, synthetic sweetening, and coloring agents, with some indication as to probable toxicity. The testing requirements for organic dyes before they can be used as food additives are discussed, and some of the relationships between structure and carcinogenic activity in the azo dyes are reviewed, since most of the food additives fall into this category. On the basis of the toxicological information available, the organic dyes are divided into 3 classes: those which have been studied adequately with respect to safety (none of the food additives are in this class), those which are currently under investigation and will soon be in Class I, and those which are considered potentially dangerous and inadmissible. Several examples of each class are given; among the possibly dangerous organic dyes are Sudan I and III, p-dimethylaminoazobenzene, yellows OB and AB, orange I, aminoazotoluene, Trypan blue, eosin and a number of triphenylmethanes.

- 3-29 IMMUNOLOGICAL DISORDERS DURING THE
COURSE OF LEUKEMIA AND HEMATOSARCOMA.
(Fr.) Miller, D. G. (Sloan Kettering Inst.,
New York). Rev. Franc. Etud. Clin. Biol. 7(10):
1112-1125, 1962.

In an extensive review of the literature, the author discusses the effect of the various types of leukemia, polycythemia, reticulosarcoma,

myeloma, lymphoma and Hodgkin's disease on the immune responses of the body, specifically on the inflammatory response, phagocytosis, the level of circulating antibodies, delayed hypersensitivity reactions, the titers of complement and properdin, general resistance to infection, tolerance to homologous bone marrow transplants and heterografts of skin, the incidence of secondary neoplasms and the development of autoimmunological processes. Deficiencies in γ -globulin and of circulating antibodies are most commonly associated with the lymphoproliferative diseases, while Hodgkin's disease is often accompanied by delayed hypersensitivity reactions. In the myeloproliferative diseases, functionally abnormal granulocytes are found. A consideration of these immunological disorders leads the author to the hypothesis that leukemia and Hodgkin's disease themselves may be considered autoimmunological processes. (89 references)

- 63-30 RELATIONSHIPS BETWEEN GASTRIC ULCER AND
CANCER. (Sp.) Silva Risopatrón, L.
Hosp. Vina d. Mar 18(2):102-106, 1962.

After pointing out the differences of opinion in the literature concerning the possible degeneration of a gastric ulcer, the author contrasts the pathological development and histological picture of ulcers and cancer and suggests that their simultaneous presence in a particular stomach may be the result of a variety of processes. On the basis of his own experience, he reports that ulceration is found in 30% of all cases of gastric cancer, that both gastric ulcers and cancer are found in 9% of cases resected for ulcer and 15% of those resected for cancer, and that a diagnosis of degenerated ulcer may be made in 3% of cases resected for ulcer and 5% of those with cancer. He suggests that the prognostic factors operating in degenerated ulcers are the same as those taken into consideration in gastric cancer.

- 63-31 ONCOGENIC VIRUSES AND CANCER. (It.)
Rowson, K. E. K. (Cancer Res. Dept.,
London Hosp. Med. Coll., England). Recenti
Progr. Med. (Roma) 33(5):369-390, 1962.

Following a brief review of the history of oncogenic viruses and a detailed review of the literature on polyoma viruses in mice, hamsters, rats, rabbits and guinea pigs and their properties *in vitro*, the author discusses the theoretical significance of the terms "virus" and "tumor cell" and outlines the relationships between viruses and cells, with particular attention to the bacteriophages and to polyoma virus. Finally, the author attempts to clarify what constitutes neoplastic change, and concludes with some remarks on the work being done in the hope of demonstrating the viral etiology of human tumors. (123 references)

- 63-32 CHEMICAL PREVENTION OF THE LESIONS DUE
TO IONIZING RADIATION. (It.) Cozza, A.

Ann. Med. Nav. (Roma) 67(6):724-740, 1962.

In this general discussion is outlined the mechanism of action of ionizing radiation in considerable detail and the attempt is made to show how all of the biological effects, from radiation sickness to the eventual appearance of leukemia, malignant neoplasms or genetic mutations, are dependent upon the initial physico-chemical lesion produced by ionized molecules on the enzyme systems or DNA of the cell. Since the effects of radiation are generally untreatable, being irreversible, they must be prevented by administering appropriate substances (reducing agents) before irradiation. Several protective substances of this type are reviewed and their mechanism of action is discussed. The possibility of the eventual discovery of agents which would reverse the effects of radiation is also mentioned. Substantial progress must await a better understanding of the elementary mechanism of action.

63-33 LONG-TERM TOXICITY AND CARCINOGENICITY.
(Fr.) Truhaut, R. Actualités Pharmacol.
15:257-306, 1963.

Before analyzing the principal circumstances under which mankind is exposed to the risk of chronic intoxication, the author reviews the factors responsible for or which facilitate the eventual appearance of long-term toxicity; the cumulative properties of the agents concerned (which depend both on their physical properties and on their chemical affinities); summation of effects; the possibility of long-term toxicity due to indirect mechanisms such as the destruction of essential dietary factors, the formation of toxic compounds from dietary components, an inhibitory effect on the intestinal flora or inhibition of the intestinal absorption of nutritive elements. Under summation of effects, particular attention is paid to the work of H. Druckrey with the carcinogens p-dimethylaminoazobenzene, p-dimethylaminostilbene, N,N-diethylnitrosamine, methylcholanthrene and 3,4-benzpyrene. The principal ways in which man can be exposed to long-term toxicity are from the incorporation of chemical agents into food (pesticides, hormones, preservatives), air pollution, occupational toxicity, the consumption of drugs and the use of cosmetics. Finally, the author makes some suggestions designed to improve the experimental techniques for evaluating the risk of long-term toxicity. (225 references)

63-34 INDUSTRIAL CANCER IN SOUTH AFRICA.
(E.) Walters, L. G. (Pneumoconiosis Res. Unit, Counc. Sci. Indust. Res., Johannesburg, South Africa). Med. Proc. (Johannesburg) 9(2):24-30, 1963.

In a review of the circumstances peculiar to the industrial development of South Africa which have influenced and will continue to influence the incidence of industrial cancer, the author points out that mining has, until recently, been the only industry in his country, so that the latent period for the appearance of most industrial cancers has not yet passed; this does not mean, however, that preventive measures should not be taken at once. The author emphasizes the incidence of silicosis, asbestosis and coal pneumoconiosis among South African miners as a contributory factor to the increased incidence of lung cancer. In addition, a number of non-mining dusty trades are now becoming more important. The author then mentions some of the other carcinogenic agents which may be encountered industrially, such as aromatic amines, arsenic, beryllium, coal tars, cobalt, chromium, nickel and soot, and reviews some of the contributory factors in the natural environment, such as cigarette smoking and air pollution; the concept of cocarcinogens and synergism is also discussed. (17 references)

63-35 STILBESTROL'S QUESTIONS. (E.) Dodds, C. (Middlesex Hosp., London, England). Pp. 321-324 in On Cancer and Hormones: Essays in Experimental Biology. Chicago, U. Chicago Press, 1962. \$8.50.

In a review devoted to the uses of and problems connected with diethylstilbestrol, mention is made that a certain stilbene derivative could be regarded as an analog of benzpyrene, and was also carcinogenic. The author feels that if we are to understand the control of cell growth, we must find an answer to the apparent lack of orderliness in the relationship between organic structure and estrogenic activity.

63-36 THE PROBLEM OF THE VIRAL ETIOLOGY OF HUMAN LEUKOSES (REVIEW). (Rus.) Bergol'ts, V. M. Probl. Gemat. 8(1):24-34, 1963.

This extensive review includes a tabular comparison of data from a number of authors on viruses isolated from various types of leukemic mouse strains. The induction of neoplasia in animals injected with nucleic acid isolated from leukemic tissue is ascribed to the presence of nucleic acid virus which is less infective than complete virus and acts as a very dilute virus. Such nucleic acid may derive from the nuclei of leukemic cells genetically "coded" for cancer. Isolated and brought into contact with normal cells, it may be incorporated by these cells and confer the "cancer stamp" on them. Another less likely hypothesis, is that cytoplasmic nucleic acid from leukemic cells may cause neoplastic transformation by introducing some altered, nonviral substance into the normal cell. (72 references)

See also abstract no. 87

PHYSICAL CARCINOGENESIS

63-37 DEMONSTRATION OF HOST RESISTANCE AGAINST SARCOMAS INDUCED BY IMPLANTATION OF CELLOPHANE FILMS IN ISOLOGOUS (SYNGENEIC) RECIPIENTS. (E.) Klein, G. (Inst. Tumor Biol., Karolinska Inst., Med. Sch., Stockholm, Sweden), G. O. Sjögren and E. Klein. Cancer Res. 23(1): 14-92, 1963.

Cells of mouse sarcomas, induced by cellophane after heavy irradiation, were injected into their autochthonous hosts, which were then challenged with serially increasing small doses (from 10^2 to 10^6) of viable, nonirradiated cells of the same tumor. No induced resistance could be demonstrated in these mice. However, in isologous hosts, similar pretreatment with irradiated tumor cells did reduce somewhat the tumor take and growth of inoculated small doses of viable tumor cells, and raised the threshold of susceptibility. Thus, where untreated controls could form tumors after inoculation with 10^3 living tumor cells, tumor induction in mice pretreated with irradiated tumor cells required doses of 10^4 and 10^5 cells. In other experiments, previous whole-body irradiation (350-400 r) of recipients reduced the threshold dose of cells that could grow into tumors; although the differences from controls showed only at low dosages of viable tumor cells. In combined *in vitro-in vivo* experiments, lymph node cells of preimmunized hosts that were resistant against low cell doses showed a certain neutralizing effect when admixed to target tumor cells. While the antigenicity of the film-induced sarcomas was relatively weak, it shows that this is not a property limited to neoplasms induced by aromatic hydrocarbons.

63-38 EXPERIMENTAL PRODUCTION OF INTRAMANDIBULAR CARCINOMA IN MICE BY MECHANICAL DAMAGE. (E.) Hollander, C. F. (Lab. Path., U. State, Leyden, Holland) and T. G. Van Rijssel. J. Nat. Cancer Inst. 30(2):337-359, 1963.

Whisker hair, V_{2a} -steel wire or nylon thread were introduced bilaterally into the alveolus of WLLF x 020 F₁ mice of both sexes before the age of 3 mo.; in the wire group, more pieces were introduced in some animals at 6 mo. of age. Because of the large diameter of the nylon thread, the alveolus was first prepared by the introduction of wire which was usually removeable after $1\frac{1}{2}$ -2 mo. The introduction of foreign material produced injury to the enamel-forming epithelium, causing it to become metaplastic. Cyst formation occurred in controls as well as in treatment groups and all groups had hair in the mandible. Incidence of carcinoma was 1/149 in controls (tumor age 15 mo.); 20/165 (12.1%) in the hair group (mean tumor age 24 mo.); 8/89 (9.1%) in the wire group (24 mo.); and 29/95 (30.3%) in the nylon group (23.4 mo.). Tumors varied from planocellular to entirely anaplastic carcinoma (often with spindle-shaped cells and abundant mitoses). In many tumors sarcomatoid transformation occurred.

Metastases in the superficial cervical lymph nodes were seen in 33% of the animals with carcinoma. These results would support the opinion that chronic irritation of epithelium provides conditions for the development of carcinoma.

63-39 EXPERIMENTAL PRODUCTION OF CARCINOMA IN THE JAW OF MICE. (E.) Van Rijssel, T. G. (Lab. Path., U. State; Leyden, Holland) and C. F. Hollander. Pp. 153-156 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

See preceding abstract. In discussion of this paper, it was stated that metastases had been found in the lungs as well as in the cervical glands.

63-40 X-RAY EXPOSURE AND MALIGNANCY. (E.) MacMahon, B. J.A.M.A. 183(8):721, 1963.

An evaluation was asked of studies made concerning the use of relatively moderate degrees of X-ray exposure for diagnostic or therapeutic purposes and subsequent incidence of malignancy. While recent studies include both positive and negative findings, there is evidence that mortality from leukemia and other cancers is about 40% higher among children exposed to diagnostic X-ray study *in utero* than among children not so exposed. This excess risk, over the first 10 yr. of life, amounts to about 1 cancer death per 2000 children exposed. This relationship in adults is much less firm; however, at least 2 studies indicate more frequent association of X-ray examination of the trunk within 5 yr. in pts. with myeloid leukemia than in pts. with lymphatic leukemia, other cancer pts., and healthy controls. It may be prudent to recognize that at the present time there is more evidence in favor of the existence of such a relationship than there is against it.

63-41 OSTEOGENIC SARCOMA IN A LUMINOUS WATCH DIAL PAINTER. (E.) Davis, C., Jr. (Presbyterian-St. Luke's Hosp., Chicago), R. G. Brown and R. W. Alexander. Arch. Surg. (Chicago) 86(2):190-195, 1963.

This case history describes the clinical manifestations and treatment of a 52-year-old female, who developed a radiation osteitis of multiple bones and an osteogenic sarcoma of the ilium with metastases. She died of bronchopneumonia 30 yr. after her occupational radiation injury (of which she was unaware). Despite surgery and palliative irradiation treatments, the primary lesion of the iliac bone progressed, with metastases to lungs, pleura, diaphragm, liver, vertebrae, and ribs. Pathological fractures, areas of increased bone density, and obliteration of joint spaces (previously treated as arthritis) were roentgenologic changes characteristic of this long-continued

internal irradiation and chronic irritation.

- 63-42 IONIZING RADIATION AND CARCINOGENESIS IN MAN. (E.) New Eng. J. Med. 268(8): 444, 1963.

In an editorial which notes the dearth of adequate information on radiation-induced carcinogenesis, attention is called to a paper in the same issue of the Journal (CRA 1(1):#43, below), and to the potential value of the data reported therein toward supplying this need.

- 63-43 THYROID CARCINOMA IN MAN AFTER EXPOSURE TO IONIZING RADIATION. A SUMMARY OF THE FINDINGS IN HIROSHIMA AND NAGASAKI. (E.) Socolow, E. L. (Mass. Gen. Hosp., Boston), A. Hashizuma, S. Neriishi and R. Niltani. New Eng. J. Med. 268(8):406-410, 1963.

In a statistical study of the comparative distribution of thyroid carcinoma diagnosed between July, 1958 and July 1961, incidence was significantly greater ($p < 0.001$) among pts. who were heavily exposed to ionizing radiation during the 1945 atomic bombings (those at a distance of less than 1399 meters from the hypocenter) than in matched groups of nonexposed pts. The 21 cases of thyroid carcinoma uncovered among approximately 15,000 pts. examined showed an age distribution with the highest frequency (42%) in the 30-39 yr. age group whereas in a general hospital population, highest frequency (42%) was in the 50-59 yr. age group. Of the 21 cases reported, 16 were men, 5 women. At the time of exposure the pts. ranged in age from 6-20 yr. The latent period after exposure can only be defined as < 13 or 15 yr. owing to the fact that all cases in this study were diagnosed only between 1958 and 1961. It is suggested that the earlier age distribution may be attributed to radiation-induced acceleration of the pathologic process.

- 63-44 X-RAY INDUCED FIBROMAS AS PRECANCEROUS STAGES OF SARCOMAS. (E.) Kröning, F. (Med. Res. Inst., Max-Planck Soc., Göttingen, Germany) and W. Eger. Pp. 683-694 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In observations extending over 6 yr., three histologically similar benign mouse fibromas, induced 18-27 mo. after irradiation of the dorsal skin of C57Bl/Kn mice with 48000 r, 7-27 mo. after transplantation became transformed in three separate instances, into malignant fibrosarcomas (one in addition developed into a carcinoma). All sarcomas were reticuloendothelial sarcomas which metastasized to the lungs (in one instance, to the heart and liver as well). It is concluded that these unstable fibromas were precursors of sarcomas, showing true tumor progression, and were not due to somatic mutation.

See also abstract no. 112

- 63-45 MALIGNANT TUMORS OF THE THYROID AS LATE EFFECT OF IRRADIATION. (E.) Uehlinger, E. (Path. Inst., U. Zurich, Switzerland). Pp. 761-766 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Among 294 thyroid malignancies found among 55,564 autopsies, one thyroid carcinoma was in a 12½-year-old female who had received irradiation therapy in the neck region at the age of 1 because of extensive hemangiomas of the skin. Two adult patients (aged 42 and 75), who developed thyroid sarcoma following repeated strumectomies for nodular goiter and carcinoma, received postoperative irradiation to the thyroid region.

- 63-46 DIFFERENCES IN THE INCIDENCE OF LYMPHOID TUMORS IN NATURALLY RESISTANT MICE FOLLOWING X-IRRADIATION ALONE OR IN COMBINATION WITH AN HOMOLOGOUS LEUKEMIC EXTRACT. (Fr.) Rivière, M. R. (Lab. Exp. Med., Inst. Sci. Cancer Res., Villejuif, Seine, France), I. Chouroulinkov, C. Marty and M. Guérin. C. R. Soc. Biol. (Paris) 156(6):1035-1038, 1962.

In groups of 120 young (4-6 wk.) and adult (4-6 mo.) mice of the resistant XLII strain, neither X-irradiation (300 r) nor i.p. injection of 0.1 ml of a lymphoma extract from AKR mice produced any cases of leukemia or lymphoid tumors, but the combination of irradiation and leukemic extract (24 hr. later) led to the appearance of lymphoid tumors in 3% of adult and 7% of young mice following a latent period of 16-28 mo. Since tumors developed only in females, the rates were actually 5% in adult and 11% in young mice. The mechanism of action of the combined treatment remains unclear.

- 63-47 DIFFERENCES IN THE INCIDENCE OF OVARIAN TUMORS IN RELATION TO THE AGE AND STRAIN OF MICE SUBJECTED TO TOTAL BODY X-IRRADIATION. (Fr.) Rivière, M. R. (Lab. Exp. Med., Inst. Sci. Cancer Res., Villejuif, Seine, France), I. Chouroulinkov, C. Lasne and M. Guérin. C. R. Soc. Biol. (Paris) 156(10):1605-1607, 1962.

Total body irradiation (300 r), after from 1 to over 2 yr., led to the appearance of ovarian tumors in young (4-6 wk.) and adult (4-6 mo.) mice. Incidence, resp., in the IC strain was 14% and 10%; XLII strain, 43% and 26%; C3He/A strain, 92% and 67%. Non-irradiated control mice showed ovarian tumors only in the C3He/A strain (6% and 9%). The histological types were mostly follicular-tubular tumors and luteomas. X-irradiation thus stimulated the development of ovarian tumors, particularly in young animals. In the IC strain where mammary tumors appear at a low spontaneous rate, irradiation of young animals decreased their incidence, whereas irradiation of adult animals increased the incidence of mammary cancers.

CHEMICAL CARCINOGENESIS

63-48 OBSERVATIONS ON TRAUMA-INDUCED NEOPLASTIC CHANGES IN THE UTERINE CERVIX OF MICE. (E.) Li Min-Hsin (Inst. Exper. Med., Chin. Acad. Med. Sci., Peking, China), Ts'ai Hai-Ying and Wei Hui-Chuan. *Chin. Med. J.* 81(12):792-799, 1962.

The effects of various treatments combined with ligation of the external os of the uterine cervix in KM mice after histological examination were graded as follows: 0, no histological change; I, epithelial hyperplasia or downgrowth of short epithelial processes; II, atypical epithelial hyperplasia, with epithelial cords extending into the stroma; III, early cancerous growth with epithelial cords extending deeply into the stroma; IV, carcinoma, with extensive invasion. In intact mice, during the 17-26 days of the experiment, at twice weekly intervals, the os was mechanically irritated by brushing and 0.01 ml of a 2% croton oil solution was instilled into the vagina: the number of mice showing no effect (0) and Stages I, II, III, and IV were: 0, 3, 14, 6, 1. In a similar group but treated 17-37 days, results were: 0, 43, 12, 3, 1. In a group of mice which were ovariectomized, estradiol benzoate (EB; 5 µg x 1, s.c.) was given 4 days later, followed after 5 days by cervical ligation and twice weekly brushing and croton oil, results were: 4, 11, 1, 1, 0. In a similar experiment in which oophorectomized mice received twice weekly doses of EB, 0.05 µg in addition to the priming dose, results were: 3, 7, 1, 0. Cervical lesions were mainly located at the site of ligation. Deciduomas developed in 1 of the mice which appeared to exhibit pseudopregnancy, indicating that the trauma produced by ligation also had some effect on the endocrine system.

63-49 INFLUENCE OF HORMONES ON CARCINOGENESIS OF UTERINE CERVIX OF MICE INDUCED BY 1-METHYLCHOLANTHRENE. (E.) Li Min-Hsin (Inst. Exper. Med., Chin. Acad. Med. Sci., Peking, China), Ts'ai Hai-Ying, Ch'en Ting-Hsien and Tsung Yung-heng. *Chin. Med. J.* 81(12):800-812, 1962.

1-Methylcholanthrene impregnated thread (MC) was inserted in the cervical canal of all experimental groups (except OeLMC) of female KM mice, 3-4 mo. old. In group EMC 42 intact mice were pretreated with estradiol benzoate (E; 15 µg/wk. x 2, s.c.) before treatment with MC (0.8 mg): 21.4% developed precancerous lesions of the cervix, 69% carcinoma, after 210 days. In group MCE, 5 wk. after MC, 90 mice received E (15 µg/wk. x 7) and results were 4.4% and 53.4%, resp. In 55 MC only controls, results were 27.4% and 65.4%, resp. In subsequent experiments the amount of MC was reduced to 0.4 mg, the periods of observation were shortened to 7, 27 and 37 days, and in some groups ovarian hormonal influence was removed by oophorectomy (O). Results were histologically evaluated as follows: 0 = no pathological change; Stage I = cervical epithelial hyperplasia and metaplasia; Stage II =

atypical metaplasia and atypical hyperplasia of the uterine cervix; Stage III = early squamous cell carcinoma; Stage IV = squamous cell carcinoma. In combined 27- and 37-day groups of OEMC (E; 15 µg/wk. started 2 days after 0 + MC) results were: 2, 6, 4, 5, 2 (carcinoma incidence, Stages III + IV (7/19) = 36.8%). In the OETMC group (E; 15 µg/wk. x 2 + testosterone (T) 2.5 mg every 3 days x 2, both started 3 days after 0 + MC), results were: 5, 8, 5, 5, 2 (28.0%). In OMC control mice (no E), results were: 6, 13, 3, 0, 3 (12.0%). In group OeCGMC (E; 0.05 µg 2 days after 0; MC, 3 days later; E was then resumed, 0.05 µg/wk. + chorionic gonadotropin (CG), 20 U, injected/wk. x 6, started 8 days after 0), results were: 14, 3, 2, 4, 4 (29.6%). In group OeMC controls, results were: 16, 6, 2, 3, 1 (14.3%). In 2 groups, MC-impregnated thread was ligated (L) in the external os. In group OeLMC (E; 5 µg 3 days after 0; followed 3 days later by LMC; then E was resumed, 1 µg/wk.), results after 39 days were: 0, 7, 3, 1, 0 (9.1%). In the parallel group OELMC (E; 15 µg/wk.) results were: 0, 3, 6, 1, 2 (25.0%). In the ETMC group, intact mice were primed with E (15 µg) before MC and 4 days later were given T (2.5 mg every 3 days x 3). Two wk. after MC, mice were given further doses of E (15 µg) and T (2.5 mg). Combined results after 37 and 90 days in the ETMC group were: 6, 22, 4, 11, 13 (42.9%). Intact mice were given progesterone (Pr; 1 mg x 4) during the 2 wk. before MC; in a 37-day experiment mice received additional Pr (1 mg/wk. x 4), in a 90-day experiment 11 similar weekly doses were given. Combined results in the PrMC group were: 9, 5, 6, 2, 6 (28.6%). Results in MC only controls were: 1, 12, 8, 4, 13 (44.7%).

63-50 COUNTERACTION BY SULPHYDRYL COMPOUNDS OF THE ENZYMIC CONVERSION OF AND THE METABOLIC LESIONS PRODUCED BY TWO CARCINOGENIC N-NITRO-SODIALKYLAMINES IN RAT LIVER. (E.) Mizrahi, I. J. (Dept. Biochem., Antoni van Leeuwenhoek-Huis, Amsterdam, The Netherlands) and P. Emmelot. *Biochem. Pharmacol.* 12(1):55-63, 1963.

Excess cysteine administration to male rats (150 mg x 2/day x 2, s.c.) led to an inhibition of the demethylation of dimethylnitrosamine (DMNA) and 4-monomethylaminoazobenzene (MAB) but not of the de-ethylation of diethylnitrosamine (DENA) and 4-monoethylaminoazobenzene (EAB) by microsomes isolated from the rat liver on the third day. Prior treatment with cysteamine (12.5 mg, i.p., followed after 1 hr. by 10 mg, i.v.), after a further 4-hr. period did not lead to any inhibition of N-dealkylation of any of the 4 substrates. In *in vitro* studies, addition of reduced glutathione (20 µM/flask) showed no inhibitory effect on the N-dealkylation of the 4 substrates by the liver microsomes of normal rats. Cysteamine and cysteine (20 µM/flask) appeared to be markedly and about equally inhibitory to the N-dealkylation of all 4 substrates. In similar experiments, when the amount of cysteine was reduced to 8 µM in the case

of EAB and MAB, and 6 μ M in the case of DMNA and DENA, the N-demethylating enzyme was still inhibited while there was no effect on the N-de-ethylating enzymes. The inhibitions of *in vitro* amino acid incorporation into liver microsomes following administration of DMNA, DENA or CB 2446 were either completely prevented or reduced following injection of cysteamine. The glycogenolysis produced in liver by i.v. cysteamine and cysteine was counteracted by DMNA and DENA.

63-51 TUMOR-SPECIFIC ANTIGENS AND THE HOMO-
GRAFT REACTION. (E.) Prehn, R. T.
(Dept. Path., U. Wash., Seattle). Am. J. Surg.
105(2):184-191, 1963.

True tumor antigenicity has now been demonstrated in several different systems in experimental animals. The immunity produced is similar to that found in the homograft reaction and much information related to homografts has applicability to tumor-immunity systems. However, extreme care is necessary in experimental work to distinguish between the two types of immunity. Thus far the tumor antigens appear to be peculiar to the particular tumor or type of tumor; on the basis of presently available evidence, there appears to be no universal cancer antigen. Some work with s.c. induced sarcomas in mice indicates that an inverse correlation exists between degree of immunity and the length of the tumor induction period. After induction with 20-methylcholanthrene, 1,2,5,6-dibenzanthracene and Millipore "fused" filter material, average length of induction (wk.) was 15, 33 and 47, resp.; average age when tumors arose was 31, 49 and 63 wk., resp.; Immunity Index (% of tumors in control mice/% of tumors in specifically immunized mice) was 3.50, 2.55 and 1.26, resp. In a spontaneous tumor of presumed longer (but not stated) latency, Immunity Index was approximately 1.1. Animal findings probably have human counterparts and tumor antigenicity may help explain some of the paradoxical behaviour of human neoplasms. The possibility of antitumor immune responses in human beings might well be considered when therapies which might damage the immune response are contemplated.

63-52 HISTOCHEMICAL AND QUANTITATIVE ANALYSIS
OF ALKALINE PHOSPHATASE DURING THE
COURSE OF EXPERIMENTAL INTRACRANIAL NEOPLASIA.
(E.) Kirsch, W. M. (Dept. Anat., Washington U.
Sch. Med., St. Louis, Mo.). Neurology (Minneapolis)
13(2):123-134, 1963.

After intracerebral implantation into C3H mice of cylindrical pellets (1 mm x 3 mm) of 20-methylcholanthrene (20-ME; 0.3 mg) fused with cholesterol, brain tumors were induced in 36/115 after 240 days. In preneoplastic animals, alkaline phosphatase was markedly diminished about the 20-ME pellets, especially in the capillary network. In 3 intracranial sarcomas as well as in 7 malignant astrocytic tumors, alkaline phosphatase activity was reduced in all cellular constituents of the tumors,

blood vessels, and glial cells; the neuropil and capillaries of the normal uninvolved brain retained their usual enzyme activities. In 4 ependymomas there was an intense generalized alkaline phosphatase reaction, both in blood vessels and tumor cells, which was greater than that of adjacent normal brain. Control cholesterol pellets were surrounded by a fibrous reaction with a normal or increased alkaline phosphatase activity. The experimentally induced brain tumors bear histochemical resemblances to human spontaneous tumors and, therefore, provide a convenient prototype for study.

63-53 CARCINOGENIC EFFECTS OF N,N'-2,7-FLUOREN-
YLENEBIS-2,2,2-TRIFLUOROACETAMIDE
(2,7-FAA-F6) ADMINISTERED ORALLY TO BUFFALO STRAIN
RATS. (E.) Morris, H. P. (NCI, Bethesda), B. P.
Wagner, F. E. Ray, H. L. Stewart and K. C. Snell.
J. Nat. Cancer Inst. 30(1):143-161, 1963.

Buffalo rats, 6 male, 14 female, starting at average ages of 4.0 and 4.3 mo., resp., were fed N,N'-2,7-fluorenylenebis-2,2,2-trifluoroacetamide (2,7-FAA-F6) until death at average ages of 14.3 and 13.0 mo., resp., so that daily average intake was 4.7 and 3.6 mg, average total intake was 1485 and 969 mg, resp. The organs most frequently involved with cancers and precancerous lesions were the mammary gland, skin, lung, submaxillary gland, glandular stomach (including 1 sarcoma), jejunum, uterus, liver, adrenal gland, ear; 2 rats developed leukemia, 3 others possible leukemia. In 6 female and 6 male control rats, at autopsy at average ages of 15.5 and 18.2 mo., resp., exhibited: 1 mammary adenoma, 4 hypophyseal adenomas in the females and 1 hepatic lymphangioma, 3 hypophyseal adenomas, and 2 adrenocortical adenomas in the males. Carcinoma of the liver was seen in 5/6 males compared to 1/14 females; however the females were exposed to the carcinogen for a shorter period of time. There was a single intraorbital neurilemmoma whose origin was obscured by the extent of the tumor. The skin tumors had a relatively long latent period. While there were many similarities to N-2-fluorenylacacetamide (2-FAA), and some differences (less atrophy of the ovary, virtually no atrophy of the testis and hypophysis), in general 2,7-FAA-F6 was less carcinogenic in terms of the number of organs involved with tumors, the number of tumors/organ, and the degree of malignancy of the tumors induced. The only real exception was that 2,7-FAA-F6 was very potent for the female mammary gland, approaching in this respect 2-FAA.

63-54 FAILURE OF INOCULATION WITH POLYOMA VIRUS
TO INFLUENCE CHEMICAL CARCINOGENESIS IN
MICE. (E.) Malmgren, R. A. (NCI, Bethesda) and
A. S. Rabson. J. Nat. Cancer Inst. 30(1):203-206,
1963.

Fifty C3H/HeN male mice at age 1 mo. received 106.8 tissue-culture infectious doses, i.p., of polyoma virus. Three wk. later, half received 20-methylcholanthrene, (20-MC), 0.5 mg, s.c.; the other half were painted on the back with 20-MC,

0.3% solution 3 x/wk. Twenty male A/LN mice were similarly infected; after 3 wk. they were treated with urethan (0.7 mg/g, i.p.). In both experiments, all polyoma-treated groups developed the same number of tumors and at the same rate as in uninfected mice treated with the same carcinogens. Polyoma virus infection therefore did not interfere with or protect against chemical carcinogenesis.

63-55 INTESTINAL MUCOSAL CHANGES INDUCED BY
 CHEMICAL CARCINOGENS. (E.) Anderson,
R. E., W. G. Diffenbaugh, E. L. Strohl and W.
Schmidtke. Presbyt. St. Luke Hosp. Med. Bull.
2(1):23-30, 1963.

Nineteen surgical implantations were made (17 of 20-methylcholanthrene and 2 of 9,10-dimethyl-1,2-benzanthracene), by introducing 1-3 capsules (approx. 60 mg) into the submucosal layer of the colon of 8 dogs and biopsied at intervals of 2-14 mo. In 2-5 mo. after implantation, submucosal abscess, necrosis, inflammation, and granuloma developed. At 6-7.5 mo., perforation of the muscularis mucosa was observed, followed during the next 7-12 mo. by mucosal ulceration (open luminal ulcer), then submucosal scarring, diverticulum formation during healing, with occasional inclusions of nests of cells in the submucosal tissues consisting of irregular cystic masses lined with mucosal epithelium. At 8.5 mo. a polypoid mucosal reaction was seen. Controls showed only normal scar tissue.

63-56 EXPERIMENTAL CARCINOGENESIS OF THE LUNG.
 INHALATION OF GASEOUS FORMALDEHYDE OR
AN AEROSOL OF COAL TAR BY C3H MICE. (E.) Horton,
A. W. (Kettering Lab. U. Cincinnati Coll. Med.,
Ohio), R. Tye and K. L. Stemmer. J. Nat. Cancer
Inst. 30(1):31-43, 1963.

Inhalation of formaldehyde by mice at levels of 0.05 and 0.10 mg/l for three 1-hr. periods each week for up to 64 wk. failed to produce squamous-cell carcinoma in the tracheobronchial tree although basal cell hyperplasia and stratification occurred more frequently than in controls; some squamous cell metaplasia was also found. At a level of 0.20 mg/l, there was a higher incidence of these changes (with in addition, atypical metaplasia) but this concentration was highly toxic and had to be terminated before the 11th treatment. After exposure to a coal tar aerosol (0.3 mg/l) for three 2-hr. periods/wk. from wk. 35-71, 5/33 mice with no pretreatment developed squamous cell tumors, one of which was a carcinoma. In a second group similarly exposed to the coal tar, but which had been subjected to formaldehyde (0.1 mg/l) during wk. 1-35, 1/26 developed a squamous-cell tumor. No abnormal histological changes were noted in 30 control mice after 82 wk.

63-57 IMMUNOHISTOCHEMICAL DIFFERENCES AMONG
 N-2-FLUORENYLACETAMIDE-INDUCED RAT
HEPATOMAS. (E.) Hiramoto, R. (Roswell Park Mem.

Inst., Buffalo), J. Jurand, J. Bernecky and D. Pressman. Cancer Res. 23(1):109-111, 1963.

Selected antihepatoma microsome antisera and a pool of antinormal rat liver microsome sera, studied by the indirect fluorescent antibody technic, were able to detect antigenic differences among several N-2-fluorenylacetamide-induced rat hepatomas from individual rats. Two antihepatoma sera out of eleven showed marked specificity in their reaction with hepatoma. After rat liver absorption, each serum was able to react only with the hepatoma against which it was prepared, and did not react with other hepatomas or with normal liver. These individual differences, and the corresponding differences between the hepatomas formed in each individual animal, account for the varied reports of staining or non-staining of hepatoma cells by antibodies against normal liver.

63-58 THE GROWTH-STIMULATING EFFECT OF TSPA
 AND 5-FU ON CELLS OF SARCOMA 180. (E.)
Abd El-Ghaffar, Y. (Cancer Res. Unit, Ein Shames
U., Cairo, Egypt). Cancer 16(1):8-12, 1963.

After *in vitro* exposure to drug for 6-8 hr., pieces of Sarcoma 180 tumor were transplanted into 4-week-old mice. Thio-tepa, 1 μ g/ml, led to earlier appearance of tumors, which after 3 and 5 wk. were 6.4 and 18.4 mm in diameter (controls were 3.1 and 9.5 mm, resp.); after 5-fluorouracil (5-FU; 0.02 mg/ml) tumors, were 11.5 and 23.4 mm in diameter, resp. (controls were 5.2 and 13.5 mm). In *in vivo* studies, drug treatment (s.c. injection daily x 10, then every other day x 10) was started on the day following implantation of mice with Sarcoma 180. While thio-tepa, 1 and 3 mg/kg/day was somewhat inhibitory, 0.1 mg/kg/day enhanced tumor growth; after day 18 and 23, tumor diameters were 24.3 and 30.1 mm, resp. (controls, 14.0 and 15.4 mm, resp.). 5-FU, 10 and 30 mg/kg/day was inhibitory while 1 mg/kg/day was stimulatory: after 18 and 23 days tumor diameters were 20.7 and 28.4 mm, resp. (controls, 13.9 and 15.4 mm, resp.). When thio-tepa (0.1 mg/kg/day) was combined with 5-FU (1 mg/kg/day), the growth stimulating effect was nearly doubled: after 18 days, tumor diameters for drugs alone were 19.4 and 19.4 mm, resp.; after combined therapy, 24.4 mm; controls, 13.1 mm. Addition of hyaluronidase (5 U.S.P. U/ml) to a stimulatory concentration of thio-tepa (not given) appeared to further enhance tumor growth.

63-59 ONCOGENIC EFFECT OF METHYLCHOLANTHRENE
 IN NEW-BORN GERM-FREE MICE. (E.)
Pollard, M. (Lobund Lab., U. Notre Dame, Ind.) and
J.-C. Salomon. Proc. Soc. Exp. Biol. Med. 112(1):
256-259, 1963.

20-Methylcholanthrene (0.1 mg, in olive oil), was injected s.c. within 18 hr. of birth into the interscapular region of 61 non-inbred Swiss-Webster mice of the 19th generation in a germ-free environment, and 54 conventionally maintained mice. After 8, 10 and 15 wk., groups of 27, 9 and 11 germ-free

surviving mice showed an average of 35, 45 and 169 surface adenomas per lung, resp. Groups of 19 and 26 treated, conventionally maintained animals after 8 and 10 wk. showed an average of 22 and 41 tumors, resp. While all treated germ-free mice developed tumors, 11% of the conventional mice remained free of tumors. No lung lesions were found in either germfree or conventional controls. Viral agents have not been detected in the adenoma tissues by electron microscopy.

- 63-60 RING CURRENTS IN 3:4-BENZOPYRENE, 1:2-BENZANTHRACENE, AND 1:2;5:6-DIBENZANTHRACENE. (E.) Memory, J. D. (U. So. Carolina, Columbia). Biochim. Biophys. Acta 66(1):168-169, 1963.

As some of the theory relating the electronic configuration of aromatic hydrocarbons to their carcinogenic potency rests on molecular-orbital calculations, it is of interest to re-examine the range of validity of molecular-orbital theory as applied to polycyclic hydrocarbons by making theoretical predictions based on the theory and which can be checked experimentally. Use was made of a modification due to McWeeny (Mol. Phys., 1(1958):175) of London's (J. Phys. Radium, 8 (1937):397) theory of diamagnetic anisotropy in aromatic molecules. Ring currents (value 1/9 for benzene) for the potent carcinogen 3:4-benzopyrene, for rings 1-5 were: 0.1338; 0.1422; 0.0933; 0.1435; and 0.1196, resp. For the mildly carcinogenic 1:2;5:6-dibenzanthracene, ring currents for rings 1-3 were: 0.1264; 0.1048; and 0.1432, resp. Ring currents for rings 1-4 of 1:2-benzanthracene were: 0.1243; 0.1412; 0.0990; and 0.1247, resp.

- 63-61 ELECTRON MICROSCOPIC STUDIES OF THE ESTROGEN-INDUCED PITUITARY TUMORS. (E.) Shimazaki, M. (Dept. Path., Wakayama Med. Coll., Japan), G. Ueda, N. Ito, H. Mukobayashi and J. Shirakawa. Wakayama Med. Rep. 7(1):1-11, 1962.

Pituitary tumors, induced in pairs of mature, young female rats by estradiol dipropionate (E, Ovahormon-depot; 0.5 mg/10 days), after 10 days, 1, 3, and 6 mo. (total doses 0.5, 1.5, 4.5, and 9.0 mg, resp.) weighed: 8.5-12.0; 12-15; 24-26; and 130-410 mg, resp. Concomitantly, the developing pituitary tumors showed progressively more chromophobic and hypertrophied parenchymal cells; the acidophils were characterized electron microscopically by a well developed endoplasmic reticulum, often whorled, and with few cytoplasmic granules. Rarely, degenerated basophils were detected. These findings tend to support the view of other workers that pituitary tumor growth is related to the stimulation of acidophils by estrogen. The enlarged Golgi bodies and nucleoli, decreased staining capacity, and well developed endoplasmic reticulum of hypertrophied acidophils indicate increased secretory activity, possibly an expression of prolactin production.

- 63-62 EFFECT OF VITAMIN E ON CARCINOGENICITY OF METHYLCHOLANTHRENE. (E.) Haber, S. L. (Dept. Path., U. Chicago) and R. W. Wissler. Proc. Soc. Exp. Biol. Med. 111(3):774-775, 1962.

After 24 wk. female C57 Leaden strain mice that had received methylcholanthrene in oil (0.1 mg, s.c.) and maintained on regular laboratory chow developed 13 fibrosarcomas (incidence of 54%), while a treated group maintained on laboratory chow with added Vitamin E (0.67 g/kg) developed 8 fibrosarcomas (incidence of 30%). No tumors developed in 70 control animals which were fed the Vitamin E-enriched diet. In a parallel experiment with 130 C57 Black male mice, controls fed only the Vitamin E-enriched diet (7.0 g/kg) after 26 wk. developed 2 lymphomas (incidence of 6%). The methylcholanthrene-treated group on a normal diet developed 9 fibrosarcomas, 3 lymphomas and 1 hepatoma (total 13, incidence of 33% after correction for early deaths); those on the high-Vitamin E diet developed 7 fibrosarcomas, 1 lymphoma and 1 squamous carcinoma (total 9, a corrected incidence of 21%). The statistical significance of these results approximates the 93% level.

- 63-63 MAST CELL REACTION DURING CHEMICAL SKIN CARCINOGENESIS OF THE LIZARD LACERTA AGILIS. (E.) Stolk, A. (Dept. Histol., Free U. Amsterdam, The Netherlands). Experientia 19(1):20-21, 1963.

Skin papillomas were induced by a single application of 9:10-dimethyl-1:2-benzanthracene (0.05 ml of a 0.5% solution in acetone) to the backs of adult female lizards (Lacerta agilis) after a mean 50-day latent period. Examined by fluorescence microscopy, about 18 days after painting, the mast cells of the skin acquired a peculiar golden-yellow fluorescence; with time they appeared to be smaller than those in normal skin, were poorly metachromatic and showed few granules. These effects were localized within the treated region. Analysis of the skin for 5-hydroxytryptamine (normal level, 0.3 µg/g) revealed a content of 1.85 µg between 18-25 days, 2.5 µg, 25-46 days and 4.5 µg in the fully developed papilloma. Skin which had been subjected to long extraction with acetone showed no fluorescence. Thus, it would seem that the fluorescence of the mast cells in induced papillomas may be due to the accumulation of hydroxytryptamine, confirming the findings by others in mice.

- 63-64 MITOTIC DIVISION OF TISSUE MAST CELLS AS INDICATED BY THE UPTAKE OF TRITIATED THYMIDINE. (E.) Asboe-Hansen, G. (Rigshosp. U. Copenhagen, Denmark) and H. Levi. Acta Path. Microbiol. Scand. 56(3):241-244, 1962.

Skin papillomas developed in 10% of 6-week-old female white St/EH2 mice 6-7 wk. after the skin of the back was painted 4 times with 9,10-dimethyl-1,2 benzanthrane (0.5 ml of 0.5% benzene

solution); sections of these induced tumors showed dense accumulation of mast cells. Tumor-bearers, 3-10 days after the first papilloma appeared, received tritiated thymidine (5 μ C/g, i.p.). All autoradiograms of tumor sections, made 0.5-20 hr. after injection, showed labeling of mast cells. About 1% of the cells showed significant nuclear labeling, and 1-2% cytoplasmic labeling. It was concluded that at least 1% of the mast cells of the connective tissue below the induced papillomas had incorporated tritiated thymidine during the 30-60 minutes when it was available, indicating that DNA synthesis and mitotic division had occurred.

63-65 OVARIAN TUMOURS INDUCED BY A STERILIZING STEROID. (E.) Lipschutz, A. (Nat. Health Service, Santiago, Chile), R. Iglesias and S. Salinas. Nature (Lond.) 196:946-948, 1962.

Ovarian granulosa-cell tumors were induced in 8/33 BALB mice maintained with 19-norprogesterone (N; given as s.c. implanted pellet for 375-559 days with pellet reimplanted every 6-7 mo.); induced sterility for 13 or more mo. (which corresponds to approximately 25 yr. in women); ovarian tumors did not occur in the normal controls. The granulosa-cell tumor was unilateral in 7/8 of the N-treated animals and bilateral in 1/8. The ovaries of 17/33 of the animals also contained an abundant number of lutein cells which are similar to those of the luteoma that occurs in mice with subtotal castration and intrasplenic ovarian transplantation. While the tumors described were experimental in origin, the tumors so obtained are similar to spontaneous ovarian tumors described in 11 different strains of mice and rats.

63-66 TUMOR-PROMOTING PROPERTIES OF ANTHRALIN (1,8,9-ANTHRATRIOL). (E.) Bock, F. G. (Roswell Park Mem. Inst., Springville, N. Y.) and R. Burns. J. Nat. Cancer Inst. 30(2):393-397, 1963.

CR Swiss and C57/St mice at 55 days of age were given an initiating stimulus of 9,10-dimethyl-1,2-benzanthracene (DMBA; 125 μ g) applied to the shaved dorsal skin. During the second period of treatment, which commenced 25 days later and continued for 32-48 wk., test compounds were applied topically 5 x/wk. Anthralin (1,8,9-anthracetriol; 0.01%) in Swiss mice induced tumors in 2/14 (14%); at 0.033% incidence was 17/30 (57%). Applied once a wk., 0.033% induced tumors in 2/15. In 57 mice, anthralin, applied 5 x/wk., at 0.01% was ineffective; 0.033% induced tumors in 6/13 (46%). In DMBA-pretreated Swiss mice, croton oil at 0.33 and 1.0% produced tumors in all 31 animals treated; 0.10 and 0.033% induced tumors in 15/16 and 8/16, resp. In C57 mice, croton oil at 1.0% induced tumors in 12/13 (93%). DMBA used alone was ineffective; anthralin alone gave rise to tumor in 1/30 Swiss, and 0/39 C57 mice. Most tumors were typical papillomas, but among the 103 tumor-bearing mice were 16 with squamous

carcinoma as evidenced by local invasion (8/36 among mice treated with DMBA and anthralin, and 8/66 among the tumor-bearing mice treated with croton oil).

63-67 SERUM LACTIC DEHYDROGENASE LEVELS IN MICE DURING THE DEVELOPMENT OF AUTOCHTHONOUS AND CHEMICALLY INDUCED TUMORS. (E.) Crispens, C. G., Jr. (Dept. Anat., U. Md. Sch. Med., Baltimore). J. Nat. Cancer Inst. 30(2):361-365, 1963.

In C3H/Fg mice with either spontaneous fibrosarcomas or methylcholanthrene-induced lymphatic leukemia, the tumors were palpable as much as 4 and 11 wk., resp., before significant increases in serum lactic dehydrogenase (LDH) were recorded. Tumor size was not correlated with enzymatic activity in mice with chemically induced tumors. The LDH time curves for both groups were similar. Maximal enzyme levels occurred 2 wk. before death; a few days before death, there was an abrupt fall in serum LDH activity.

62-68 CARCINOGENIC ACTIVITY OF CIGARETTE SMOKE CONDENSATE. (E.) Moore, G. E. (Buffalo). J.A.M.A. 183(8):715-717, 1963.

In commenting on the article "Carcinogenic activity of cigarette smoke condensate" (Drs. Bock, Moore, Dowd, and Clark, J.A.M.A. 181:668, 1962) R. J. Needles questions the logic of comparing painting the backs of mice with smoke condensate and the effect of smoking cigarettes on the entire area of the respiratory membrane of the average man (condensate from 8.3 cigarettes/mouse = 18,000 cigarettes for a man). In reply it was stated that the ratio of exposed mouse skin to the area of human bronchial mucosa effectively exposed to cigarette smoke is 1:6. In the experiments referred to, each mouse during a year was painted with less than 50 g of smoke tar; a heavy smoker may inhale 200-400 g of smoke tar each year for many years.

63-69 NEOPLASMS OF RAT URINARY BLADDER AND LIVER. RATS FED 2-ACETYLAMINOFLUORENE AND INDOLE. (E.) Oyasu, R. (Presbyterian-St. Luke's Hosp., Chicago), D. A. Miller, J. H. McDonald and G. M. Hass. Arch. Path. 75(2):184-190, 1963.

2-Acetoaminofluorene (AAF; 0.06% + standard diet) in 26/26 induced rapidly developing malignant liver tumors (metastatic in 14), 5/26 developed benign bladder tumors; 8 other neoplasms were also found. None survived more than 7½ mo. (average 194 days). Upon the addition of indole (1.6% and 3.2%), during months 6-9, benign bladder tumors developed in 1/6 and 0/8, resp.; none developed malignant tumors. During the same time benign liver tumors developed in 4/6 and 6/8; malignant liver tumors developed in 1/6 and 0/8, resp. After 10 + mo. benign bladder tumors were induced in 5/25 and 3/19; malignant in 12/25 and 9/19,

resp. After 10 + mo., benign liver tumors developed in 10/25 and 15/19; malignant in 15/25 and 4/19, resp. Average survival in the two groups was 337 and 373 days, resp. Rats treated only with 3.2% indole developed no neoplasms; their average survival was 430 days. It appears that AAF + indole-induction of bladder cancer is positively correlated with both the degree of liver injury and also with cystadenomatous neoplasia of the liver.

- 63-70 AUTORADIOGRAPHIC LOCALIZATION OF PROTEIN-BOUND AMINOAZO DYES. (E.) Hughes, P. E. (Dept. Path., U. Melbourne, Australia) *Exp. Cell Res.* 29(4):327-342, 1963.

Dye localization in the rat liver, after 14 days' feeding of tritiated 3'-methyl-4-dimethylaminoazobenzene (3'-MeDAB; 0.063% in the diet, S.A. 628.3 mC/mM) 2 days after partial hepatectomy was studied autoradiographically by the examination of 10,000 high power fields. Mean liver cell grain densities were: parenchyma, 62.2; bile duct, 15.4; Kupfer cells, 23.5; for the non-carcinogenic 2-MeDAB, the counts were similar. For both agents, 90% of the grains lay over the cytoplasm: grain density was much reduced over chromatin. In rats treated with colchicine + 3'-MeDAB there was no association of bound dye with mitotic spindle fibers. In fact, cells in mitosis showed a reduced grain count (30.5 as against interphase cells with 62.2). This difference was not found with 2-MeDAB. While regenerating liver examined 24 hr. after injection of a single large dose of 3'-MeDAB showed the same general labeling as after feeding, grain counts in cells undergoing mitosis were quite variable. The author feels that the cells in areas of decreased dye binding (seen only after treatment with carcinogen) might be placed at a growth advantage.

- 63-71 DISTRIBUTION OF PROTEIN-BOUND DYE IN SUBCELLULAR FRACTIONS FROM RATS LIVER DURING THE ADMINISTRATION OF 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE. (E.) Yamada, T. (Dept. Biophys., Fac. Sci., U. Tokyo, Japan), M. Matsumoto and H. Terayama. *Exp. Cell Res.* 29(4):153-161, 1963.

In the rat, after treatment with 3'-methyl-4-dimethylaminoazobenzene (25 mg x 1, p.o.), dye-binding in subcellular fractions of the liver ($\mu\text{g}/100 \text{ mg}$ protein), after 5 and 40 hr. was: supernatant, 0.9 and 1.2; deoxycholate (DCA)-soluble microsome fraction, 0.8 and 0.5; DCA-insoluble microsome fraction, 0.6 and 0.5, resp. Likewise, in prolonged feeding (0.06%, rice coated with dye dissolved in corn oil) the concentration in the supernatant rose to a peak of 6.5 μg at 1 wk., in the DCA-soluble and DCA-insoluble fractions peaks were at 3 μg and 4 μg , resp., after 2 wk., both decreasing to about 2 μg for the remainder of the 12-wk. experimental period. During this time, some rats had developed tumors in the liver. It is suggested, as a possible mechanism of carcinogenesis, that the continuous binding of

the carcinogenic dye to the proteins of the ribosomes might indirectly induce some irreversible change in the activity of the genes.

- 63-72 THE CARCINOGENIC ACTION OF CERTAIN LACTONES AND CHEMICALLY RELATED SUBSTANCES. (E.) Dickens, F. (Middlesex Hosp. Med. Sch., London, England). Pp. 107-120 in *On Cancer and Hormones: Essays in Experimental Biology*. Chicago, U. Chicago Press, 1962, \$8.50.

β -Propiolactone (1.0 and 0.1 mg, in arachis oil x 2/wk., s.c.; this was $\frac{1}{2}$ and $\frac{1}{20}$ th of the dose employed in earlier work) induced local, transplantable, sarcomas in 14/14 rats that survived more than 25 wk.: none appeared in 16 oil-injected controls. Two derivatives, the sparingly soluble α -carboxy- β -phenyl- and α,α -diphenyl- β -propiolactone (in 1 mg doses) each induced sarcomas in 1/5 rats; that of the latter compound was transplantable. Crystalline penicillin G sodium (which also contains a heterocyclic 4-membered ring), at 2 mg x 2/wk., in arachis oil, induced malignant tumors in 2/8 rats which survived 59-84 wk. and 3/12 given approximately $\frac{1}{3}$ million U/rat. The antibiotic, patulin (clavacin) in oil (0.2 mg 2x/wk. s.c.) induced local sarcomas in 6/8 rats which survived 58 + wk.; 1/3 were successfully transplanted. Closely related penicillic acid at 1.0 mg dose induced local sarcomas in 4/4 rats after 48-67 wk.; 3/4 were transplanted successfully. 5-Hydroxy-2-hexenoic acid lactone (parasorbic acid), injected for 30 wk. at doses of 2 mg, induced local tumors in 4/11 survivors at 60 wk. This lactone has been considered the probable cause of tumor growth inhibition by various crude plant extracts. Of 3 synthetic γ -lactones, methyl protoanemonin (the most active one) at 2 mg doses induced local sarcomas in 3/5 rats after 61 wk., and transplants of 2/3 grew well; 2-hexenoic γ -lactone produced local sarcomas in 2/4 surviving rats after 79 wk. (1/2 showed poor transplantability). Results were negative with α -angelica lactone and with γ -valerolactone. All the carcinogenically active 5-membered lactones possessed either α,β -unsaturation or an external unsaturated bond attached to the ring at position 4, or both. The presence of such bonds, or of the highly strained 4-membered ring, renders the lactonic grouping highly reactive, not necessarily to hydrolysis by water molecules, but to nucleophilic attack.

- 62-73 AN AETIOLOGICAL STUDY OF LUNG TUMOURS IN MICE. (E.) Peacock, P. R. (Roy. Beatson Mem. Hosp., Glasgow, Scotland). Pp. 605-612 in *The Morphological Precursors of Cancer*. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

The incidence of lung tumors and the anatomic distribution of inhaled soot were investigated in 2 groups of C3Hf male mice, reared identically in central Glasgow except for the filtration of soot from the atmospheric environment of Group 1. The frequency of lung and liver tumors in this strain was about 20% in males over 500 days old. Tumor incidence for 74 and 72 that survived more than

500 days in Groups I and II, resp., was: lung = 20.6% and 15.3%, liver = 16.2% and 19.7%, both = 2.7% and 4.2%, showing no significant differences in tumor incidence or organ affected. However, the over-all mean survival was about 100 days greater in mice given filtered air. In Group II mice, no correlation was found between tumor incidence and either the number or the location of soot spots on the lungs. However, in mice exposed to sooty atmosphere the soot was deposited in the lymphatic system; soot spots were found more frequently in areas of the lungs covered by the ribs rather than by the intercostal muscles. A useful technic for in situ lung fixation is described.

63-74 ON THE SERIAL CHANGES OF ¹³¹I-LABELED SERUM PROTEIN INCORPORATED IN RATS BEARING DAB-INDUCED HEPATOMA. (Jap.) Inui, S. (1st. Dept. Int. Med., Gifu Prefect. Med. Coll., Japan) and S. Goto. Nisshin Igaku (Jap. J. Med. Prog.) 48(2):99-105, 1961.

One hr. after administration of ¹³¹I-labeled homologous serum protein (1 ml i.v. = 4.05 x 10⁶ cpm) to normal rats and rats bearing p-dimethylaminoazobenzene (DAB)- induced hepatoma, radioactivity of the serum protein fractions of both groups were very high but decreased after 24 hr. to 1/11 and 1/6, resp., of the 1 hr. values. Serum values then showed gradual decrease for several days with marked decrease after 10 days. After 24 hr. radioactivity of the hepatoma protein fraction was 1/20 of the 1 hr. value, while comparable decrease in normal liver protein was only 1/9. Hepatoma protein showed rather higher activity (compared to normal) from 48 hr. to 5 days after injection; both fell to low levels after 10 days.

63-75 ACCELERATED MAMMARY TUMOR DEVELOPMENT IN C3H MICE FED AN IODINE-DEFICIENT DIET. (E.) McAlexander, R. A. (Dept. Surg., U. Wash. Sch. Med., Seattle), J. K. Stevenson, P. D. Olch, G. M. Bogardus, J. W. Finley and H. N. Harkins. Surg. Forum 13:105-106, 1962.

Among 68 female C3H mice (a high spontaneous mammary tumor strain) fed a goitrogenic, iodine-deficient diet, 21% developed mammary tumors after 57 wk., while tumors developed in only 9% of 64 controls. First tumor onset was at 23 wk. Death before mammary tumor development occurred in 69% of mice on normal diet, and in 62% of the iodine-deficient mice, many of the latter dying earlier and all showing large goiters at autopsy. It is concluded that iodine deficiency accelerates mammary tumor formation in C3H mice. Abnormally high levels of thyrotropic hormones have been shown to cause excess production of estrogen and mammotropic hormone when the pituitary was intact, resulting in mammary hyperplasia.

63-76 CHANGES OF UTERUS EPITHELIUM INDUCED IN MICE BY 20-METHYLCHOLANTHRENE. (E.) Olivi, M. (Inst. Morbid Anat., Div. Cancer Res.,

U. Perugia, Italy), G. Barbieri and I. Paoletti. Pp. 467-477 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

20-Methylcholanthrene was applied to groups of 43, 35 and 47 virgin BALB/c mice as follows: Groups I and II, drug dissolved in beeswax was used to impregnate sections of cotton cord (each with about 1.75 mg) which were introduced into the cervical canal at 60 and 107 days of age, resp.; these mice were sacrificed 152 and 68 days later, resp. Group III, 0.1 ml of a 5% solution in olive oil was injected into the right uterine horn, after which the extremities were tied off; these mice were treated at 107 days of age and sacrificed 93 days later. Incidence (%) of uterine lesions (for Groups I, II and III) was: hyperplasia of cervical epithelium - 4.7, 28.6 and 8.5; cervical cancer - 74.4, 62.9, and 4.3; glandular hyperplasia - 11.6, 80.0, and 38.3; squamous metaplasia of glandular epithelium - 20.9, 45.7, and 40.4; cancer of the uterine horn - 7.0, 14.3, and 36.2. In Group III, 23.4% developed uterine sarcomas. Cytological study of vaginal smears of Group I mice revealed 74.5% with anomalous cells, which first appeared 34 days after start of treatment; certain of these cells, which were very large, elongated and with many nuclear and chromatin abnormalities (a more coarsely granular pattern) were considered as pre-cancerous cells, since they were observed early in those mice in which cancer developed. Tumors could be palpated about 50 days after application of the carcinogen.

63-77 INDUCTION AND OTHER PROBLEMS OF TAR CANCER. (E.) Deelman, H. T. (Lab. Morbid Anat., U. Amsterdam, The Netherlands). Pp. 69-73 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Induction of skin cancers by repeated skin painting with tar was shown to be a cumulative effect (summation of irritation) in mice, where an average of 18 applications of the carcinogen produced tumors regardless of the time interval between applications (daily to weekly), and even when applications were interrupted for some weeks. When the size of the tar field was varied from 20 x 25 mm down to 2½ x 25 mm, it was found that the smaller the tar field, the greater was the number of tumors induced: small areas of application also led to reduced systemic toxicity. By grafting of young-tumor-bearing skin to partly untreated areas, it was demonstrated that inductive growth (the transformation into malignant cells of normal epithelial cells adjacent to a tumor) occurred only on areas where the carcinogen had been applied. This restriction did not apply to advanced tumors.

63-78 OBSERVATIONS UPON THE INDUCTION OF SUBCUTANEOUS SARCOMATA IN RATS. (E.) Walpole, A. L. (Res. Dept., Imperial Chem. Indust. Ltd., Alderley Park, Macclesfield, Cheshire,

England). Pp. 83-88 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

No tumors developed in 2 groups of 12 male and 12 female Wistar rats given Tween 60 (0.5 ml/100 g of a 6% solution, x 1/wk. x 16 or 28, s.c., resp.) + a regular diet: there was high mortality in the 28-week group from wk. 75-100. In parallel groups in which 2-acetylaminofluorene (AAF) was fed in the diet at levels of 0.03% and 0.05%, resp., starting 2 wk. before the injections for 19 and 7 wk., resp., 7 and 6, local sarcomas appeared at the injection sites between wk. 24-60 and 54-85, resp. After similar injections of Cellofas B (2%; sodium salt of carboxymethyl cellulose) during wk. 1-19, 4 rats developed local sarcomas between wk. 58-68; in a parallel group in which AAF, 0.03% was added to the diet, 11 developed local sarcomas between wk. 33-62. In a group which received only 0.5% carrageenin for 21 wk., 10 rats developed local sarcomas between wk. 51-88; in the group also given AAF, 0.03% in the diet for 19 wk., 11 rats developed sarcomas between wk. 34-60. In the latter group there were 10 deaths between wk. 30-50. In control groups of 24 males and 24 females treated only with AAF (0.05% in the diet for 7 wk.) and a similar group fed AAF 0.03% for 19 wk., only 1 female (fed at the higher level) developed a fibrosarcoma. In groups of 12 male and 12 female rats, no tumors developed in groups which received: (1) 0.5 ml distilled water, s.c. x 1/wk. x 19 + control diet; (2) distilled water injections + AAF, 0.05% in the diet for 7 wk.; (3) distilled water injections for 25 wk.; (4) similar group + AAF, 0.03%, for 22 wk. It is obvious that AAF accelerates the appearance and increases the final yield of tumors at the site of injection of Tween 60, Cellofas B or carrageenin. The role of the latter substances appears to be limited to tumor promotion.

63-79 MODIFICATIONS IN THE ORGANIZATION OF MACROMOLECULES OF LIVER CELL CYTOPLASM DURING NORMAL AND NEOPLASTIC PROLIFERATION. (E.) Di Marco, A. (Dept. Exp. Chemother., Tumor Inst., Milan, Italy). Pp. 219-227 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Electrophoretic patterns on agar showed identical nucleoprotein fractions with positive migration in homogenates of normal and regenerating rat liver, neoplastic (AH 130) cells, and liver of rats fed dimethylaminoazobenzene (DAB), which were analogous to those seen in the microsomes of differentiated liver treated with sodium deoxycholate. Components of these fractions (found also in the supernatant of tumor cell homogenate at 78,000 g), were further identified by optical density, measurements at different wave lengths, and by study of immunological reactions. The microsomes from neoplastic cells showed a deficiency in cholesterol synthesis, decrease in the phospholipid:protein and phospholipid:RNA

ratios, and an increase in the RNA:protein ratio, compared to normal liver tissue. Liver from DAB-fed rats showed a decrease in the ratio of phospholipid:protein but not of phospholipid:RNA. The author suggests that the difference between neoplastic and differentiated cells, in respect to the quantity of the nucleoprotein fraction elaborated, appears to be due to failure of the neoplastic cell to synthesize completely the endoplasmic reticulum, to which this nucleoprotein fraction is strongly associated in differentiated cells.

63-80 THE ACID MUCOPOLYSACCHARIDES OF THE SKIN FOLLOWING EXPERIMENTAL INDUCTION OF CUTANEOUS TUMORS. (It.) Prodi, G. (Inst. Gen. Path., U. Bologna, Italy) and R. David. Sperimentale 112(5):360-364, 1962.

A comparative chemical study of the acid mucopolysaccharides (MPS) in the skin of normal rabbits and rabbits treated topically twice a week for 1 month by 9,10-dimethyl-1,2-benzanthracene (0.3% solution in acetone) showed no qualitative differences between the 2 groups; however, the ratio of hyaluronic acid/chondroitin sulfuric acid was increased to 2.7 in treated rabbits compared to 1.3 in controls as indicated by changes in the levels of hexosamines (glucosamine + galactosamine) in MPS NaCl extracts, from 57% and 43% in controls to 73% and 27% in treated animals at 0.4 and 1.2 N NaCl concentrations, resp.

63-81 THE USE OF METHYLCHOLANTHRENE-INDUCED SKIN CARCINOMA OF THE MOUSE IN RADIO-BIOLOGY. (E.) Evans, J. C. (Dept. Radiol., Albert Einstein Coll. Med., N. Y.). Radiology 80(2):309-311, 1963.

During experiments in which cutaneous carcinomas were being induced in mice by the application of a saturated solution of 20-methylcholanthrene in benzene to the dorsal skin, for the purpose of creating more suitable test objects for experimental radiotherapy, it was noted that the incidence of localized squamous carcinoma was higher and the latent period was shorter in the inbred CBA strain than in random-bred albino Swiss mice. Epilation occurred at 1 wk., gross neoplasms appeared at about 20 wk., and the lesions caused death in 3-4 mo. in all untreated cases. In some animals treated successfully by irradiation, a new malignancy, usually a fibrosarcoma, was later found at the old site.

63-82 EFFECT OF 5-BIS-(2-CHLOROETHYL)-AMINO-URACIL ON METABOLISM OF AMINO ACIDS IN NORMAL AND PRECANCEROUS RAT LIVER. (E.) Burke, W. T. (Dept. Biochem., W. Va. U. Med. Ctr., Morgantown). Proc. Soc. Exp. Biol. Med. 111(3): 811-813, 1962.

Studies of the incorporation of lysine-6- C^{14} , glutamic acid-U- C^{14} and glutamine-U- C^{14} into the

plasma proteins and liver acid-soluble and total proteins, as well as of the expiration of $C^{14}O_2$, during a 4-hr. perfusion of isolated livers from either normal male rats or rats fed a diet containing 0.06% of 3'-methyl-4-dimethylaminoazobenzene for 8-10 wk. showed that administration of an azo-dye increases both the capacity of the liver to synthesize acid-soluble proteins, as well as the conversion of glutamine- C^{14} to $C^{14}O_2$, but decreases the production of CO_2 from the other amino acids. In azo dye fed rats, uracil mustard reduced by 50% lysine incorporation into total protein. Addition of uracil mustard to the perfusate had no effect on CO_2 production or the incorporation of amino acids into plasma proteins, but decreased the synthesis of acid-soluble liver protein in both normal and carcinogen-treated rats.

63-83 PRECANCEROUS CHANGES IN THE URINARY BLADDER. (E.) Bonser, G. M. (Dept. Exp. Path., U. Leeds Sch. Med., England). Pp. 435-439 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Examination of the urinary tract and bladder in 59 rabbits fed a variety of compounds to the limit of tolerance for periods up to 6 yr. revealed only metaplasia in those given auramine, papilloma in 1/19 given 2-naphthylamine, and definite carcinomas among those fed 1-phenylazo-2-naphthol (1/7), benzidine (1/9), 4-aminodiphenyl or 2-acetamidofluorene. The histology of the normal and precancerous rabbit bladder is compared, with emphasis on hyperplasia and metaplasia; glandular metaplasia at the ureteric orifice was seen in 11 of 26 treated rabbits in which the orifices were examined, and in 1/7 controls. The results show that all of the different stages in the progression of the epithelium to the malignant state are likely to be multifocal, and that bladder tumors arise only from a hyperplastic epithelium. Glandular metaplasia probably plays a role in the etiology of bladder cancer. The advantages of bladder tumors in the study of carcinogenesis are outlined.

63-84 INHIBITION OF VISCERAL TUMORS BY KERATOACANTHOMAS IN MICE. (E.) Corbett, M. B. (Sect. Derm., U. So. Calif., Los Angeles) and L. M. Solomon. J. Invest. Derm. 40(1):9-10, 1963.

Of 27 virgin female mice, C3H Strong strain, aged $5\frac{1}{2}$ mo., painted on the dorsal skin with 9,10-dimethyl-1,2-benzanthracene (1% in lanolin-mineral oil), 16 treated for up to 4 wk. died at up to $5\frac{1}{2}$ mo. without lesions. A group of 11 that survived 8 wk. of treatment developed 16 cutaneous tumors. Four of these mice that survived to 16 mo. of age had keratoacanthomas which regressed 8-12 wk. after the last painting; upon histological examination, 3/4 showed no internal or external pathological changes. The breasts of all

4 were normal to palpation. Of 10 control mice, 7 died of unknown causes at the end of 16 wk. without evidence of any neoplastic lesions; 3 which survived 11 mo. were free of lesions.

63-85 EXPERIMENTAL INDUCTION OF PRECANCER AND CANCER OF THE STOMACH. (Rus.) Solov'ev, A. A. (Inst. Norm. and Path. Physiol., USSR Acad. Med. Sci., Moscow), E. D. Klimenko, N. A. Nilova, O. M. Pozdnyakov. Biull. Eksp. Biol. Med. 55(1): 81-85, 1963.

Capsules of 9,10-dimethyl-1,2-benzanthracene (DMBA; 5 mg in 10% paraffin) were implanted in the anterior wall of the pyloric region of the stomach of 22 rats, with simultaneous ligation of the pancreaticoduodenal veins. The depot carcinogen caused multiple neoplasms of the adjacent gastric mucosa, ranging in size from barely visible lesions to nodules 2-5 mm in diameter and, in 1 case, involvement of almost the whole mucosa. Histologically, these changes appeared as proliferations of the glandular epithelium, which persisted even after the carcinogen had been eliminated (4-6 mo. after implantation). Activation after 16-18 mo. of some of these foci, which exhibited marked destructive and infiltrative growth and high mitotic activity, emphasized the malignant nature of these proliferations.

63-86 CHANGES IN THE SUBCUTANEOUS CONNECTIVE TISSUE OF RATS INDUCED WITH SMALL DOSES OF 7,12-DIMETHYL-BENZO (α) ANTHRACENE. (Rus.) Vasil'ev, Iu. M. (Inst. Exp. Clin. Oncol., Acad. Med. Sci., Moscow). Vop. Onkol. 9(1):37-41, 1963.

Doses of 0.01, 0.1 and 1.0 mg of 9,10-dimethyl-1,2-benzanthracene (paraffinized pellets planted s.c.) in rats all caused similar initial changes (lymphoid infiltration). However, the subsequent accumulation of atypical collagen around the depot carcinogen regressed (at 2-3 mo.) after the 0.1 mg dose, and was not seen after the 0.01 mg dose. After 1.0 mg doses, the atypical collagen progressed through marked dystrophic changes in the ground substance to precancerous foci of atypical fibroblasts. Tumors developed in 10/15 rats which survived 5+ mo. after the 1.0 mg dose, but in only 2/19 rats given 0.1 mg, and then only after 8 and 12 mo., resp.

63-87 MORPHOLOGICAL PRECURSORS OF MALIGNANT TUMORS OF THE BRAIN. (E.) Avtsyn, A. P. (N. N. Burdenko Inst. Neurosurg. Acad. Med. Sci., Moscow, USSR). Pp. 667-670 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

After direct injection of 9,10-dimethyl-1,2-benzanthracene (DMBA; in olive oil, no dose) into the brains of 55 mice, no tumors developed, but there was some minimal inflammatory changes and edema and proliferation of glial cells which developed hyperchromatic nuclei at later stages (173-195 days after administration). Two other series in rodents

were reviewed. DMBA in olive oil, injected on day 13 or 19 of gestation into the brains of rat embryos, induced in the 10% of survivors some developmental abnormalities of the brain, but no tumors. Crystalline pellets of DMBA (dosage not stated) introduced into the brains of 24 C57Bl mice, caused first, local inhibition of connective tissue and astrocytes and increased vessel permeability. Later, a zone of edema and demyelination formed around the pellet, still later astrocytes proliferated. Tumors developed around the pellet in 120-300 days. Included were gliomas of varied cell composition and malignancy.

- 63-88 THE INDUCTION OF PULMONARY TUMORS IN BALB/c MICE BY ORAL ADMINISTRATION OF ISONIAZID. (E.) Biancifiore, C. (Inst. Morbid Anat., U. Perugia, Italy) and R. Ribacchi. Pp. 635-642 in *The Morphological Precursors of Cancer*. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Isoniazid, (2.0 mg/day p.o., as a 2% aqueous solution, total of 520 mg in 320 days) in 60 virgin female BALB/c mice (which does not carry the milk factor), induced pulmonary tumors in all of the 38 mice which survived for 46 wk. after the start of treatment; average age at death was 370 days. The other 22 mice died in the first few days due to technical accidents. Of the 144 pulmonary tumors found at necropsy, 134 were adenomas (72 solid, 62 papillary), 6 were adenomas undergoing transition to malignancy, and 4 were carcinomas. Of 216 untreated virgins or breeders, 125 survived from 61-121 wk.; none had pulmonary tumors. These findings are of interest, considering the widespread use of isoniazid in the treatment of human disease.

- 63-89 CLINICAL STUDIES IN LEUKEMIA-REVIEW OF 100 CASES. (E.) Vasavada, P. S. (Hemat. Dept., Dept. Med., M. G. M. Med. Coll., Indore, India), A. Ali and D. P. Mukerji. *J. Assn. Physicians India* 10(12):677-682, 1962.

In this clinical review of 100 cases of leukemia admitted during the period 1954-1961, it is stated that there was no history of exposure or susceptibility to leukemogenic agents in the series.

- 63-90 FIXATION ON CELL PROTEINS OF RADIOCARBON AND TRITIUM-LABELLED 1,2,3,4-DIBENZ-ANTHRACENE. (Fr.) Daudel, P. (Radium Inst., Paris) and A. M. Ferraz. *C. R. Acad. Sci. (Paris)* 256(2):538-539, 1963.

1,2,3,4-Dibenzanthracene labeled with tritium in the 9 and 10 positions and with C^{14} in the 10 position, was applied to the skin of Radium Institute strain XVII nc mice in a dosage of about 200 μ g in 0.2 ml benzene. After extraction of the proteins and digestion with hyamine hydroxide 10X, the ratios of tritium/radioactive carbon activity in the original hydrocarbon and in that fixed on the skin proteins of treated rats were

approximately the same: 0.92 ± 0.09 and 0.97 ± 0.09 , resp. Since previous work suggested that carbons are not lost from the hydrocarbon skeleton during the skin fixation, the present data suggest that hydrogen atoms are also not lost. The results are compatible with an addition reaction occurring by a mechanism analogous to that of a diene synthesis.

- 63-91 CHANGES IN DNA CONTENT DURING HEPATIC REGENERATION. CLINICAL AND EXPERIMENTAL DATA. (Fr.) Laumonier, R. (Dept. Path. Anat., Sch. Med., Rouen, France.) and R. Laquerriere. *Rev. Int. Hepat.* 12(5):633-654, 1962.

As part of extensive research on the changes in DNA content in liver cells during cirrhosis, hepatitis and hepatoma in man and following various types of liver damage in mice, rats and guinea pigs, the authors studied the effect of daily applications of benzidine (3% in benzene) to the lumbar skin in Wistar rats. After treatment for 15 days, jaundice due to toxic hepatitis appeared, followed by a latent period of 2-4 mo. and then a neoplastic phase during which the animals developed malignant tumors, primarily in the liver (60% of all tumors were hepatomas). Histograms of the liver tissue during the precancerous phases revealed first a gradual disappearance of diploid cells (clear-cut by 3 wk. after administration) with increasing polyploidy to an equilibrium of 4 and 8-ploid forms. Marked disorganized accumulation of DNA was observed only after tumor appearance. Intracellular DNA distribution was found to be very similar in viral hepatitis, hepatic regeneration after partial hepatectomy and in the precancerous phase of carcinogenesis. Endocrine factors (growth hormone, ACTH and cortisone) as well as vitamin B₁₂ play a role in stimulating the accumulation of DNA similar to that observed in liver regeneration. In addition, injections of a macromolecular fraction from plasma of rats hepatectomized or treated with benzidine produced tetraploidy in the livers of untreated animals. The plasma factor was present only transiently in hepatectomized animals but persisted throughout the precancerous phase in those treated with benzidine.

- 63-92 DIFFUSE CARCINOMATOSIS IN A PATIENT SUBJECTED TO INTRAVENOUS INJECTIONS OF THOROTRAST 25 YEARS EARLIER. (It.) Pisano, M. (Inst. Clin. Gen. Surg., U. Cagliari, Italy) and F. Sforza. *Collana di Monografie (Miscellanea Chir.) Rass. Med. Sarda* 6:67-87, 1961.

A 45-year-old woman who had received 3 i.v. injections of Thorotrast (75 ml in 3 days) 25 yr. before for radiographic visualization studies developed edema at the site of the injections (inner side of the left elbow) which regressed after hot pack applications. The pt. remained well for 17 yr., when a large abscess appeared at the same site followed by appearance of a fistula, which opened from time to time with the escape of fragments of

calcareous substance. Three years later, inflammation of the same region developed, accompanied by fever and generalized malaise (which responded to treatment), however, the patient began to suffer severe pain in the thigh, calf, and sole of the right foot, accompanied by edema of the same extremity. Her phlebitis responded to anticoagulants and antibiotics, but a few days after discharge she developed severe joint pain in the hand, shoulder, and hip, with a painless swelling of the right eyelid and, later, erythema and edema of the affected joints. In addition, she lost about 10 kg in 6 mo. Radiographic and scintillographic studies showed diffuse carcinomatosis with a high localization of Thorotrast in the liver and spleen. A tumor removed from the inner lid was an adenocarcinoma; no thorium or radioactivity was detected in tumor sections. Studies of other sites were refused by the pt. It was felt the primary site was in the liver. The pt. died at home with a clinical picture of neoplastic cachexia.

63-93 THE ETIOPATHOGENESIS OF HEPATOMA IN HATCHERY RAINBOW TROUT. (It.) Ghittino, P. (Inst. Gen. Path., U. Torino, Italy) and F. Ceretto. Tumori 48(6):393-409, 1962.

Histological studies of the liver during the development of hepatoma in hatchery-raised trout showed that only in rainbow trout was there a gradual accumulation of ceroid in the hepatocytes and histiocytes, leading to a distinctive type of hepatic lipid degeneration. In other areas of the liver parenchyma, there was a gradual progression from nodular hyperplasia to diffuse regenerative proliferation, adenoma and finally hepatic carcinoma capable of metastasizing to other organs. On the basis of their findings and an extensive review of the literature, the authors conclude that this neoplasm is the result of the special diets used in fish hatcheries. Although it is possible that the commercial diet contains a carcinogen, it seems more probable that deficiencies in the diet lead to hepatocytic degeneration followed by regenerative hyperplastic phenomena. (21 references)

63-94 THE EFFECT OF ALLOXAN DIABETES ON THE GROWTH OF EXPERIMENTAL TUMOR TRANSPLANTS. (It.) Tinozzi, F. P. (Inst. Gen. Clin. Surg., U. Pavia, Italy) and A. Pannella. Arch. De Vecchi Anat. Path. 37(1):1-11, 1962.

Subcutaneous homotransplants of a 3 week-old 20-methylcholanthrene-induced tumor were made in 60 adult albino rats, 40 of which were previously rendered diabetic by injections of alloxan (40 or 80 mg/kg) and maintained diabetic with alloxan throughout the experiment. Within 5-8 days, visible tumors had developed in 15/20 non-diabetic rats, which were sacrificed at 10 days, but in none of the rats given alloxan. Histological

studies of the inoculation site in 45 surviving experimental rats, sacrificed after 120 days, revealed only necrotic tissue and no tumor growth. Histological changes in the liver, pancreas and spleen of the diabetic rats are described. It thus appears that alloxan diabetes inhibits the growth and development of transplanted tumors.

63-95 THE LEUKEMOGENIC EFFECT OF BENZENE. (It.) Saita, G. (Occupational Med. Clin., U. Milan, Italy) and E. C. Vigliani. Med. Lavoro 53(10):581-586, 1962.

Among 36 cases of blood dyscrasia due to benzene examined at the authors' clinic between 1942 and 1961, there were 2 with erythrocytopenia, 5 with both erythrocytopenia and leukopenia, 4 with leukopenia and thrombocytopenia, 20 with pancytopenia, 1 with a leukemoid reaction and 4 with acute leukemia (2 previously unpublished); there were no cases of typical chronic myeloid or lymphatic leukemia. Detailed reports of the 4 cases showed a general prevalence of microhemocytoblastic elements with phases of leukopenia. Indeed, benzene-induced leukemia probably begins with hypoplasia or aplasia, followed eventually by a neoplastic process. As shown by 1 case in which there was a 12-yr. lag period between exposure to benzene and onset of leukemia, additional mutagenic stimuli may be required for the eventual manifestation of the original effect of benzene. The authors suggest that many fatal cases diagnosed as bone marrow aplasia or atrophy may actually be in the leukopenic phase of acute leukemia.

63-96 EFFECTS OF HYDROCORTISONE AND X-IRRADIATION ON SPONTANEOUS LEUKEMOGENESIS IN AKR MICE. (Fr.) Duplan, J. F. (Pasteur Lab., Rad. Inst., Paris). C. R. Soc. Biol (Paris) 156(5):779-782, 1962.

Administration of cortisol (0.5 mg/day x 6 i.m.) to AKR mice between the ages of 65 and 75 days had little effect on the incidence of lymphoid leukemia (69% compared to 76% in controls) but delayed its onset; average survival time was 348 days (controls, 283 days). When 2 groups of similar mice were subjected to total-body X-irradiation (800 r) and then given isologous bone marrow, transplants (10⁷ cells) from mice treated with cortisone were less effective in preserving life than transplants from normal mice (36.9% and 62.5% 30-day survivors, resp.), but the untreated and cortisone-treated bone marrow had essentially the same effect in reducing the incidence of leukemia (33% and 25%, resp.), without, however, delaying its onset (average survival time was 291 and 265 days, resp., controls 283 days). Cortisone therefore seems to have no direct effect on the lymphoid hematopoietic cells but delays the onset of spontaneous leukemia by an indirect mechanism, probably by disturbing the adrenal-thymus equilibrium.

See also abstract no. 134

VIRAL CARCINOGENESIS

- 63-97 FURTHER EXPERIMENTS WITH A LEUKAEMOGENIC INDUCER PRESENT IN B5 TUMOUR. (E.) Hlavayová, E. (Oncol. Res. Inst., Bratislava, CSSR), P. Kossey, J. Smida and F. Svec. Neoplasma 9(5):457-463, 1962.

The cell-free supernatant of B5 tumor from the rat, injected s.c. into the same strain within 48 hr. of birth led to development of leukemia in 8/72 (11%), after an average latent period of 536 days. In the same group 83% developed cirrhosis + hepatitis; their mean survival time was 497 days. Incidence of leukemia in rats injected with a mitochondrial fraction or a microsomal fraction was 11/139 (8%) and 6/97 (6%), resp.; average survival was 513 and 502 days, resp. Incidence of cirrhosis + hepatitis in the two groups was 84% and 71%, resp.; average survival was 477 and 505 days, resp. In the supernatant, mitochondrial and microsomal groups, there developed 4, 3 and 3 other malignancies, resp. Among the 25 treated animals that developed leukemia, 20 also developed cirrhosis or hepatitis. In controls there developed 2/95 leukemias (average survival 616 days); 1 animal developed cirrhosis and there was 4 other malignancies. When newborn rats were given 3-6 injections at weekly intervals of the supernatant fraction, 12/85 (14%) developed leukemia (average survival 441 days) and 93% hepatitis + cirrhosis (average survival 527 days) and 2 showed other malignancies. In order to test the influence of implanted tumor on subsequent development of leukemia in groups of 107, 98 and 68 animals, tumor mass was extirpated 1, 2, or 3 times, resp.: survivors numbered 90, 66 and 28, resp. and incidence of leukemia was 13%, 12% and 11%, resp. Mean survival in the 3 groups was 508, 352 and 251 days, resp. Incidence of hepatitis + cirrhosis was 55%, 56% and 64%, resp. Paralytic rats of the same sex, one of which was implanted with B5 tumor 3-5 wk. after union, were disconnected when the tumor approached the terminal stage and the tumor free partner was observed until spontaneous death. Of 10 animals that survived a sufficiently long period, leukemia + cirrhosis of the liver was found simultaneously in 3 of them; 4 others showed only cirrhosis of the liver.

- 63-98 INFECTIVITY EXPERIMENTS WITH NUCLEIC ACIDS OF THE SHOPE RABBIT PAPILLOMA AND DERIVED CARCINOMAS. (E.) Hodes, M. E. (Dept. Med., Ind. U. Med. Ctr., Indianapolis), C. G. Palmer, L. E. Beaty, M. K. Swenson and J. D. Hubbard. J. Nat. Cancer Inst. 39(1):1-14, 1963.

Treatment of Shope papilloma tissue with sodium lauryl sulfate and sodium-p-aminosalicylate, followed by extraction with phenol, yielded a material that induced papillomas in wild and domestic rabbits in the absence of deoxyribonuclease. A comparison of the infectivity of the saline and phenol extracts of 13 separate preparations suggests that only virus-producing tumors yielded infectious DNA. The infective

moiety, DNA, was precipitable by alcohol and could be freed of most of the residual protein and RNA. This material resisted heating at 100° for 10-30 minutes. Attempts to isolate infectious DNA from the Vx2 or Vx7 carcinomas were negative.

- 63-99 DISTRIBUTION OF POLYOMA VIRUS ANTIBODIES IN JAPAN. (E.) Kondo, T. (Dept. Surg., Nagoya U. Sch. Med., Japan) and H. Matsuura. Proc. Soc. Exp. Biol. Med. 112(1):170-173, 1963.

Of 12 mouse colonies in Japan surveyed for polyoma virus infection, only one was found to be infected. In this colony, 4 infected strains (A, CBA, C3H and Hrrh), were originally from the United States, and it is thought that they may have acquired latent infection before being brought into Japan: two strains (DD and DM) showed no infection.

- 63-100 PATHOGENIC POTENCY AND HOST RANGE OF THE MOUSE LEUKEMIA VIRUS. (E.) Gross, L. (VA Hosp., Bronx, N. Y.). Acta Haemat. 29(1):1-15, 1963.

Passage A leukemic virus (initially isolated from spontaneous Ak mouse leukemia, and then passed serially through newborn C3H mice), in C3H/Bittner strain, C57BR/cd and Balb/c mice induced leukemia in 88-99%; incidence in C3H/Andervont subline, random bred Swiss and strain I was 65-79%. The most common type of induced leukemia was lymphatic, although incidence of stem-cell leukemia was appreciable. Only Balb/c mice showed an appreciable incidence of myeloid leukemia. Centrifuged, cell-free extracts, prepared from C3H mice sacrificed 1-7 hr. after initial inoculation of passage A virus, were found to be leukemogenic, and induced leukemia in 81-100% of inoculated 1-5-day-old C3H mice. When virus was harvested 22 hr. after inoculation, incidence of leukemia in bioassay animals was 19%. Extracts prepared 1-3 days after inoculation contained practically no virus. Virus reappeared about 1 wk. after original inoculation, and after 15 days, incidence of leukemia in bioassay animals was 86% and 30 days after inoculation rose to 94%.

- 63-101 ELECTRON MICROSCOPIC AND BIOASSAY STUDIES ON A MURINE LEUKEMIA VIRUS (RAUSCHER): PRELIMINARY REPORT. (E.) Zeigel, R. F. (NCI, Bethesda) and F. J. Rauscher. J. Nat. Cancer Inst. 30(1):207-210, 1963.

After electron microscopy of the lipid layer (top), supernatant (middle) and resuspended pellet centrifugation fractions of the plasma of mice with virus-induced leukemia, only the pellet fraction contained "Rauscher" virus particles (which are described and illustrated). In 2 experiments, after adjustment of all fractions to a concentration of 0.05 g equivalents of plasma/ml, infectivity tests utilizing 0.1 ml/mouse revealed significantly greater

infection in the pellet fraction (100% and 100%, resp.) than in the lipid layer (71% and 83%, resp.) or the supernatant (67% and 9%, resp.). Time to palpation of tumors was also shorter in mice injected with the pellet fraction. The same relative differences were seen when the plasma was adjusted to 0.0005 g equivalents/ml, before injection.

63-102 MALIGNANCY OF POLYOMA VIRUS INFECTION IN MICE IN RELATION TO STRESS. (E.)

Rasmussen, A. F. (Dept. Infect. Dis., U. Calif. Sch. Med., Los Angeles), W. H. Hildemann and M. Sellers. *J. Nat. Cancer Inst.* 30(1):101-112, 1963.

Webster-Swiss (BRVS) mice (135) inoculated at birth (intracardiac route) with polyoma virus, then systemically stressed by avoidance learning or high frequency sound beginning 5-6 wk. later, and observed for 487 days, showed no significant difference from their (69) unstressed controls in the over-all incidence, extent or location of tumors, in survival time, or in the development of hemagglutination-inhibition antibodies. However, the frequency of overt tumors was slightly diminished in the unstressed mice (probably not significantly). The virus-induced malignancies reduced the median lifespan by at least two-thirds in all groups, and the cumulative mortality curves all showed the same log-normal distribution, though the wide range of survival times (56-415 days) reflects a highly variable disease process. The non-tumorous survivors (3 stressed, 2 unstressed) all showed high titers of antibodies. Of the tumor-bearers, 81% had multiple tumors at death, and tumors of salivary gland and lung were most frequent (62-65%), while kidney, skeletal, and s.c. tumors were found in 20%, 23% and 19%, resp. The lack of effect of stress on malignancy might be due to the time lag between virus inoculation and stress application, the virus-induced neoplastic transformation being presumably accomplished before stress application.

63-103 POLYOMA VIRUS AND L CELL RELATIONSHIP.

1. SOME CHARACTERISTICS OF A CELL LINE PERISTENTLY INFECTED WITH POLYOMA VIRUS. (E.)

Hare, J. D. (Dept. Microbiol., U. Rochester, N.Y.), P. Balduzzi and H. R. Morgan. *J. Nat. Cancer Inst.* 30(1):45-56, 1963.

Clone 929, derived from strain L cells, originally infected with 2 TCID₅₀ of polyoma virus (PV; strain 210) per cell and grown in Eagle's basal medium with 3% horse serum, has been maintained for 2 yr. supporting active viral proliferation without evidence of cytopathic effect. This infected cell line, LP, when injected i.m. into C3H male mice, resulted in no tumor development. There was no measurable difference in ability to produce tumors in the cheek pouches of cortisone-treated hamsters between the carrier line when compared to the parental cell line. The infected line could be grown in modified Eagle's medium without serum for at least 18 days and continued to

produce monolayers that were as thick and healthy as at the beginning and continued to produce quantities of hemagglutinins similar to cultures grown in the same medium supplemented with serum. This suggests that neither specific antibody nor non-specific viral inhibitors in the sera used for supplementation was of importance in maintaining the balance between virus and cell as had been shown necessary for the persistence of PV and Coxsackie B3 virus in HeLa cells.

63-104 THE ISOLATION OF POLYOMA VIRUS FROM MAMMARY CANCER IN MICE. (E.)

Leykina, F. I. (Dept. Tumor Etiol., Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR, Moscow) and Z. I. Merekalova. *Vop. Onkol. (Eng.)* 7(12):5-9, 1961.

During an attempt to isolate the virus of mouse mammary cancer by tissue culture, 2 strains of polyoma virus were isolated from mammary gland extracts of C3HA high-cancer line and from tissue extracts of C57 x C3Hf mice. Upon infection of mouse embryo fibroblast cultures, cytopathogenic changes appeared after 3 passages, and the culture fluid gave specific hemagglutination reactions; activity was retained after passage through a Seitz filter. The electron microscope revealed large numbers of globular particles not seen in control cultures. Identity of the isolated viruses was further confirmed by cross hemagglutination inhibition reactions with sera from guinea pigs immunized with SE-polyoma virus and between polyoma virus and immune sera prepared with the isolated viruses.

63-105 STUDIES ON THE LYTIC INTERACTION AND CELL TRANSFORMATION WITH A LARGE- AND A SMALL-PLAQUE MUTANT POLYOMA VIRUS. (E.)

Medina, D. (Weizmann Inst. Sci., Rehovoth, Israel) and L. Sachs. *Virology* 19(2):127-139, 1963.

The comparative lytic efficiency of small-plaque (SP2) and large-plaque (BP5) polyoma virus mutants was determined from growth curves of 1-day-old secondary cultures containing 1×10^6 cells, inoculated with 0.1 ml of each stock virus at a virus: cell ratio of 10 plaque forming units (PFU)/cell. (Virus titration was by plaque assay on C57BL/6 secondary mouse embryo monolayers.) The total virus (TV) content of both mutants, on mouse embryo monolayers, increased between 24 and 36 hr., but at 72 hr. value for BP5 was 1.7×10^8 PFU; for SP2, 1.4×10^9 PFU. The SP2 mutant also showed greater TV increase on hamster embryo cells. SP2 was also more efficient in virus adsorption during the 3 hr infection period. The percentage of SP2-infected mouse embryo cells was 3.8-7 times higher than after infection with BP5; in hamster cells, yield was 4.2 to 20 times higher. Average virus yield per virus-yielding cell was equal for the 2 mutants ($2-4 \times 10^3$ PFU). The small plaque size of SP2 showed no change with addition to the agar nutrient overlay of either DEAE-dextran or protamine. In the study of cell transformation, the percentage of transformed clones (PTC) was

determined by cloning cultures of hamster cells after exposure to virus at 20 PFU/cell. PTC for BP5 was 0.1%-0.4%; for SP2, 0.8%-2.0%. Comparable results were obtained after multiple exposures to the virus, and after a single exposure to a more concentrated inoculum (1000 PFU/cell). However, PTC was increased to 10.0% for SP2 and 3.0% for BP5 in cultures maintained at 24° C for 24 hr. before or after exposure to the virus. These results indicate that the rate of polyoma virus-induced cell transformation can be altered by choice of viral mutant and changes of culture conditions

63-106 THE ROLE OF THE THYMUS IN POLYOMA VIRUS INFECTION. (E.) Kodama, M. (Roswell Park Mem. Inst., Buffalo) and G. E. Moore. *J. Nat. Cancer Inst.* 30(2):225-239, 1963.

To clarify host-virus relationship in polyoma virus infection, virus from a single culture pool was inoculated i.v. into AKR and C3H mice and F₁ hybrids within 24 hr. after birth; half were thymectomized (TH) 2 wk. later. Mortality for infected nonTH-AKR mice rose continuously until day 160 (52% of those who survived 60 days) after which time the death rate decreased significantly. At 160 days, mortality in TH-AKR mice was 27%. This initial rise in mortality was also seen in infected nonTH-A/C mice but not in infected nonTH-C3H and C/A mice. Thymectomy delayed significantly the death of infected AKR mice but not of C3H mice. Incidence of tumors in infected and non-infected AKR mice was higher than in the other groups of mice. Neither incidence nor latency of tumors were affected consistently by thymectomy. Mean latent period for development of parotid tumors in TH and nonTH-AKR mice ranged from 109-138 days; for C3H mice, 259-230 days. Incidence of leukemia in infected AKR-TH mice was 3/49, in nonTH mice 6/60; incidence in noninfected mice was 1/31 and 10/42, resp. Among the remaining 3 groups of infected mice, only 1 nonTH-A/C developed leukemia. Hybrids whose mothers were AKR mice showed a high sensitivity to virus and the ameliorating effect of thymectomy; this was not true of hybrids with C3H mothers. It is concluded that there is a close correlation between the predisposition of AKR mice for leukemia and their sensitivity to polyoma virus infection, and that the thymus gland is partly, if not entirely, responsible for the high sensitivity.

63-107 RAPID INTRACEREBRAL PASSAGE AND RECOVERY OF MOLONEY LEUKEMIA VIRUS FROM MOUSE BRAIN TISSUE. (E.) Spencer, H. J. (Mary Imogene Bassett Hosp., Cooperstown, N.Y.). *J. Nat. Cancer Inst.* 30(2):313-320, 1963.

Moloney leukemia virus was recovered in large amounts from brain tissue harvested 7 days after intracerebral infection of newborn BALB/c mice; after 16 further passages at 7-day intervals, virulence of this virus Line 2 was markedly increased. With a 3-day harvest interval, amount

of virus recovered was small, and serial passage resulted in rapid disappearance of leukemogenic activity. In mice infected with virus from Line 2, passage 9, high mortality of 98-100% and an incidence of 80-85% of leukemia was found after 7-29 days; an overtly leukemic mouse after 62 days showed high virus level in the brain. There was no indication of neurotropic adaptation of the Line 2 virus or of other qualitative changes during 16 serial intracerebral passages; virus was readily recovered from visceral lymphatic tumor tissue. Appreciable amounts of virus were recovered from the brains of mice that had been infected i.p. The available data are consistent with the hypothesis that the brain might function as a nonre-active reservoir of virus production throughout the course of the disease.

63-108 STUDIES OF VARIATION IN ONCOGENICITY OF POLYOMA VIRUS RELATED TO DIFFERENCES IN CELL CULTURE MEDIA. (E.) Rabson, A. S. (NCI, Bethesda) and L. W. Law. *J. Nat. Cancer Inst.* 30(2):367-375, 1963.

Strain M polyoma virus, passaged in cultures of P388 D₁ cells grown in a medium containing 20% autoclaved nonfat milk, had low oncogenic potency in mice: after 104.9 and 103.8 tissue culture infectious doses (TCID₅₀) in 72 and 42 C3Hf/Bi mice, only 6.9 and 14%, resp., developed polyoma type tumors after average latent periods of 4.8 and 5.6 mo., resp. After 6 passages of M polyoma virus in a medium containing 40% human serum and 60% mixture #199, this S polyoma virus was injected into the same strain of mice. After 104.8 and 103.8 TCID₅₀, 35/35 and 29/29, resp., exhibited polyoma type tumors with average latency of 2.3 and 2.5 mo., resp. After 102.8 and 101.8 TCID₅₀, 34/36 (94%) and 19/21 (91%), resp., developed tumors with average latent periods of 2.3 and 4.2 mo., resp. With a TCID₅₀ dose of < 1, 2/17 (12%) developed tumors after a mean latent period of 6 mo. In studies of plaque morphology, in 7 different experiments, the M strains contained 0-10% large (2-4 mm) plaques and 90-100% small (0.5-1.0 mm) plaques; the S strains contained 28-50% large plaques and 50-72% small plaques.

63-109 RESISTANCE OF THE CHORIO-ALLANTOIC MEMBRANE OF CHICK EMBRYOS TO ROUS SARCOMA AND MH2 RETICULOENDOTHELIOMA VIRUSES. (E.) Dhaliwal, S. S. (Dept. Zool., U. Malaya, Kuala Lumpur). *J. Nat. Cancer Inst.* 39(2):323-336, 1963.

The chorio-allantoic membrane (CAM) of New Hampshire, Kok strain chick embryos was more resistant to Rous sarcoma virus (RSV) and MH2 virus than other strains tested. White Leghorn, Kok, was more resistant to RSV than to MH2; strain Australorp, Kok, was resistant to RSV and moderately resistant to MH2. After treatment of the embryos and day-old chicks of the various strains with serial dilutions of RSV, no correlation was found to resistance of the chorio-allantoic membranes. While the serum from both White Leghorn and New

Hampshire Red hens neutralized RSV to some extent, no difference was noted between the 2 strains. When White Leghorn, Kok, embryos were inoculated with 2.7 or 3.2 log pock-forming units (pfu)/ml, it was found that the number of pocks were abnormally distributed. When the pock count was plotted on a logarithmic scale against the cumulative percentage for virus titer of log 3.2 pfu/ml, the pocks fell on a straight line only in membranes with more than 80 pocks. This indicates that some of the CAMs with less than 80 pocks were resistant and nonreactive at low virus titer. This was confirmed by analysis of results at the lower virus titer, when only membranes with less than 20 pocks fell outside the straight line, and then not significantly so. Reciprocal crosses between two of the susceptible strains (White Leghorn and Australorp) and the resistant New Hampshire, Kok strain, showed that resistance to RSV and MH2 virus is dominant and not sex-linked.

63-110 STEPS IN THE NEOPLASTIC TRANSFORMATION OF HAMSTER EMBRYO CELLS BY POLYOMA VIRUS. (E.) Vogt, M. (Calif. Inst. Tech., Pasadena) and R. Dulbecco. *Proc. Nat. Acad. Sci. USA* 49(2):171-179, 1963.

At various times (2-24 days) after infection with polyoma virus ("large-plaque" type) of secondary hamster embryo cultures, grown in a combined Eagle's, Puck's N16 and NCTC 109 medium, single cultures were trypsinized and used to start groups of sparse subcultures (these were grown for 7 days in the presence of 20% fetal bovine serum; thereafter on regular medium). Focal lines were picked out with the aid of small glass cylinders which helped to isolate the foci so as to carry over as few untransformed cells as possible; presumably each culture was derived from a single transformed cell. Two types of control cultures were utilized: nonfocal lines, started from cells outside the glass cylinders; and lines handled in the same manner as the experimental lines but without infection. Clones formed by the cells of the focal lines could be divided into two main morphological groups: (1) "Thin" clones, in which the cells grew mainly in a single layer, were refringent and randomly oriented. (2) "Dense" clones, in which the cells were piled up in many layers, showed variable morphology: some had a uniform dense center while others had heavy strands or nodules (there was a greater proportion of the latter clones in later transfers). Clones from nonfocal and control lines were consistently monolayers; the cells were thin and transparent and showed a regular arrangement and hence were readily distinguished from the thin clones. Transplantability into 20-day-old hamsters of the cells of the focal lines was low at early transfers and increased with time, parallel to the development of clones of larger size, and increase in proportion of dense clones. Two lines of evidence indicate that the dense clone is derived from the cells of the thin clones. If precursors of the dense clones had been present throughout the sparse cultures, they

should have become evident in non-focal lines, which was never observed. Further, after 2 wk. of culturing of a line derived from a single cell of the thin clone, dense clones appeared. No infectious polyoma virus could be demonstrated in the 3rd and 6th transfer of the focal lines. The presence of unusually high numbers of dead cells in cultures of the focal lines at a time when no polyoma virus could be detected prompted an investigation of chromatid breakage. The proportion of dead cells correlated well with the proportion of mitoses which contained chromatid bridges. This proportion was strikingly high (53-84%) at the early transfers. Similar examination of non-focal and control lines revealed a significantly smaller proportion of mitoses with bridges than in the focal lines.

63-111 INHERITANCE OF SUSCEPTIBILITY TO FRIEND MOUSE LEUKEMIA VIRUS. (E.) Odaka, T. (Dept. Oncol., Inst. Infect. Dis., U. Tokyo, Japan), and T. Yamamoto. *Japan. J. Exp. Med.* 32(5): 405-413, 1962.

Susceptibility to the Friend virus was studied by crossing susceptible RF mice with resistant C57BL/6 mice. After virus inoculation, spleen enlargement and increase in nucleated blood cell number were chosen as the criteria for susceptibility. In terms of spleen weight after infection, all F₁ mice, one-half of the backcross to C57BL/6, all the backcross to RF, and "most" of the F₁ mice showed enlargement. In terms of nucleated blood cells followed over a 3-week period after infection, all F₂, half of the backcross offspring and 3/4 of the F₂ showed an increase in number. This indicates that the susceptibility is dependent mainly on a single dominant gene. There was no linkage with susceptibility and hair color or sex. Incomplete susceptibility in some of the crosses is ascribed to minor genes or physiologic background variability. One suggested possible mechanism of gene action is, that a critical quantitative level of virus must be attained to induce spleen enlargement.

63-112 DNA SYNTHESIS IN X-IRRADIATED CULTURES INFECTED WITH POLYOMA VIRUS. (E.) Minowada, J. (Roswell Park Mem. Inst., Buffalo) and G. E. Moore. *Exp. Cell Res.* 29(4):31-35, 1963

Mouse embryo tissue cultures, exposed to 10,000 or 2,000 r of X-irradiation, inoculated 1 and 2 days later with polyoma virus, and fed for 1 hr. with tritiated thymidine 24 hr. before harvest, showed on autoradiographic analysis, 8 and 6 days later, resp., a much higher percentage of labeled cells in infected (89.0 and 79.3) than in irradiated, uninfected (19.5 and 12.8) cultures. One hr. after infection, the percentage of labeled cells was 17.1 and 9.8 vs. 0.8 and 1.0. Hemagglutination titer varied between 120-160 in infected cultures. Since cytopathogenic damage to the irradiated cultures was considerable, and no

mitoses were seen, the increased DNA synthesis probably represents newly synthesized viral DNA.

- 63-113 PATHOGENESIS OF A VIRUS-INDUCED LEUKEMIA IN RATS. (E.) Dunn, T. B. (NCI, Bethesda) and J. B. Moloney. Pp. 259-268 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In a study of the development of the Moloney virus-induced leukemia of rats, the only organs that appeared to be significantly altered compared to controls were the spleen and the bone marrow (both of which underwent hyperplasia), and the thymus. An early change in the thymus was a slight relative increase in the medulla. Some (not all) lobules, then showed another change, the appearance of a uniform population of large, pale cells which replaced the normal architecture; by this time the thrombocytes in the cortex were no longer prominent. The thymus was considered neoplastic when the normal architecture over a considerable area was lost and when many large, uniform basophilic cells with numerous mitotic figures were found. A special morphologic feature in the virus-induced leukemia in these rats was the aggregation of vacuolated cells, centrally located in the area once occupied by Hassall's bodies. These aggregations were usually surrounded by the large, basophilic cells. When neoplastic cells extended beyond the thymus capsule, it was the paler cells at the periphery that extended outward into the surrounding adipose tissue and other structures. By the time the neoplastic process reached this stage, the spleen and many other organs were infiltrated with neoplastic lymphocytes.

- 63-114 OBSERVATIONS ON THE ONCOGENIC EFFECT OF POLYOMA VIRUS. (It.) Balduzzi, P. (Inst. Microbiol., U. Florence) and G. Weber. Sperimentale 112(5):376-385, 1962.

Mouse embryonic tissue (0.1 ml) infected with stock polyoma virus ($10^{6.5}$ ID₅₀/ml) was injected s.c. in the scapular area of 30 newborn Swiss mice. Among the 20 mice which survived 1+ yr., 6 showed macroscopic tumors 4-10 mo. after inoculation: 3 parotid (mixed), 1 s.c. fibrosarcoma, 1 thymus, and 1 osteogenic (skull). The authors emphasized the low incidence of tumors, the absence of multiple tumors and the small variety of histological types. An uninfected mother mouse developed a possibly spontaneous mammary adenocarcinoma approximately 7 mo. after suckling an inoculated mouse which eventually developed a s.c. fibrosarcoma. No virus could be demonstrated in tissue cultures of either the fibrosarcoma or the adenocarcinoma.

- 63-115 TUMOUR INDUCTION IN C3H AND SWISS ICR MICE BY TISSUE CULTURE PREPARATIONS OF POLYOMA VIRUS. (E.) Wallace, R. (Lederle Lab.,

Pearl River, N.Y.), E. L. Jungherr and A. W. Moyer. Nature (Lond.) 197:298-299, 1963.

In two mouse strains inoculated postnatally with 0.1-0.2 ml polyoma virus (strain 1956 8C, pools 71A, -B, -C, infectivity titer 10^{-6} to $10^{-6.5}$) female and male mice (percentage) with tumors after 10 mo. were, resp., for strain C3H: 75 and 30, 83 and 63, 29 and 24; for strain Swiss ICR: 12 and 6, 42 and 35, 15 and 0. The corresponding average latent period (mo.) at tumor incidence were, for C3H: 5.1 and 6.1, 3.1 and 4.7, 4.6 and 4.4; for ICR: 5.6 and 8.5, 5.7 and 5.9, 5.0 and -. Thus the C3H mice showed the higher tumor incidence and a slightly shorter latency period for tumor development. Tests for hemagglutinin inhibitors to polyoma virus in the sera of old breeders from each strain showed antibody in 33% of C3H mice and in only 9% of ICR mice; hence the relative resistance of ICR mice to tumor induction was not attributable to maternal antibodies. Incidence of the polyoma-induced neoplasms in 55 C3H and 34 Swiss ICR mice, resp. were: parotid gland tumors, 62% and 71%; mammary gland, 64% and 12%; thymus, 20% and 11%; others (kidney, bone, ovary, s.c. lipoma, sarcoma), 9% and 31%. Male C3H mice showed a high frequency of mammary carcinoma (53%). The very high relative frequency of parotid tumors in ICR, as compared with the equal frequency of parotid and mammary gland tumors in C3H, suggests that the vulnerability of individual host tissues to the oncogenic action of polyoma virus is at least in part a genetic feature of the host.

- 63-116 CONDITIONS AFFECTING TRANSFORMATION BY POLYOMA VIRUS. (E.) Stoker, M. (Inst. Virol., Glasgow U., Scotland) and P. Abel. Pp. 375-386 in Basic Mechanisms in Animal Virus Biology. V. 27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

In the *in vitro* assay procedure described, the mean transformation rate (TR; transformed colonies/total cells plated) of a stable line of hamster fibroblasts (BHK21), after 1 hr. exposure to polyoma virus (line 3) was 2.7% (range, 0.8-5.7%, in 9 experiments). TR was unaltered when the cells employed were seeded 1-7 days previously without medium change; RDE (receptor destroying enzyme) damaged cells and led to a marked fall in plating efficiency. TR was decreased after virus was treated with rabbit anti-polyoma serum. Most of the transforming activity of virus stock P54 (released from infected mouse embryo cell debris with RDE) resided in the "full" particles. Cytagglutination did not affect TR. When periods from 5-90 min. were employed for virus adsorption to cells, highest TR (3.1%) was obtained when a 60 min. adsorption period was followed by a 30-min. postadsorption period; plating efficiency also was maximal (49%). Transformation rate was directly proportional to virus concentration; at constant virus concentration (10^9 PFU/ml) TR was

not affected by variations in cell concentration (10^4 to 3×10^6 cells/ml). TR increased from 0.87% (control) to 2.90% if virus treated cells were exposed to $MgCl_2$ (0.025 M) after, but not during, adsorption. Both plating efficiency and TR of virus-treated cells increased in the presence of irradiated mouse feeder cells. Other possible limiting factors in polyoma virus transformation of cells are also discussed.

63-117 CYTOLYTIC EFFECT INDUCED BY PREPARATIONS OF ROUS SARCOMA VIRUS GROWN AT $40^\circ C$. (Fr.) Febvre, H. (Cancer Res. Inst., Villejuif, France), L. Rothschild and J. Arnoult. C. R. Acad. Sci. (Paris) 256(2):534-537, 1963.

The observations described indicate that the behavior of intracellular virus is a function of the incubation temperature. When this was raised from 37 to $40^\circ C$, a cytolytic effect--plaque formation--was noted in chick embryo cells infected with Rous sarcoma virus. The number of plaques formed was correlated to the concentration of virus and could thus be used for titration. Under the same experimental conditions, cells incubated at 37° showed the typical formation of foci of transformed cells. Similar results were obtained with Shope's fibroma virus. Electron

microscopic studies suggest that the number of intracellular virus particles is greatly increased at $40^\circ C$.

63-118 LOW MALIGNANCY OF ROUS SARCOMA CELLS AS EVIDENCED BY POOR TRANSPLANTABILITY IN TURKEYS. (E.) Bergs, V. V. (Inst. Microbiol., Rutgers U., New Brunswick, N. J.) and V. Groupe. Science 139:922-923, 1963.

Rous sarcomas, produced in 7-day-old Beltsville white turkeys with standard Rous sarcoma virus from chickens (10^4 to 10^5 pock-forming units, s.c.) and allowed to grow up to 20-60 days before removal, were implanted into the wing web of 7-44 day-old turkeys. Tumors were produced in the inoculated turkeys only by sarcoma cells which carried appreciable amounts of infectious virus, whether the transplant was homologous or isologous, and the development of new tumors could be prevented by simultaneous administration of antiviral antiserum. In addition, the few tumors produced at low virus titers grew relatively slowly, or regressed. The authors conclude that Rous sarcoma cells are not readily transplantable and that malignant growth of Rous sarcoma implants is virus-induced.

See also abstract no. 54

MISCELLANEOUS

- 63-119 BEHAVIOR OF TWO CELL STRAINS DERIVED FROM RAT RHABDOMYOSARCOMAS. (E.) Basrur, P. K. (Div. Microscopic Anat., Ontario Vet. Coll., Guelph, Ontario, Canada) and J. P. W. Gilman. J. Nat. Cancer Inst. 30(1):163-177, 1963.

Two morphologically identical rat cell strains, both derived from nickel sulfide-induced, highly malignant rhabdomyosarcomas during prolonged (9-16 mo.) serial culture, came to differ widely in morphology, in growth pattern, in rates of acid production, in chromosome constitution, and in malignancy. Both initially pleomorphic, polyploid and malignant, in the 5th month of cultivation, line ALA became altered: the cells were more homogeneous in size and shape (fibroblast-like), with a high proportion of diploid cells, a polarized growth pattern (lengthwise), and a slower drop in pH of the medium. Diploid cells increased from 12% to over 50% in the 5th mo., at which time capacity to induce malignant tumors was lost. This altered strain also produced giant multinucleate cells. Strain #79 remained pleomorphic, polyploid, aneuploid, with rapid drop of pH, requiring daily change of medium, and subcultures continued to produce rapidly growing metastatic sarcomas, with a progressive reduction in the latency period.

- 63-120 PRODUCTION OF TRANSPLANTABLE HEPATOMAS BY INTRASPLENIC IMPLANTATION OF NORMAL LIVER IN THE MOUSE. (E.) Leduc, E. H. (Dept. Biol., Brown U., Providence, R. I.) and J. W. Wilson. J. Nat. Cancer Inst. 30(1):85-99, 1963.

After intrasplenic implantation into BUB strain mice (in which no spontaneous hepatomas have been found) of liver from 7-day-old mice; liver containing hyperplastic nodules from donors exposed to carbon tetrachloride; regenerating liver, 48 hr. after partial hepatectomy; and cholangiole-laden liver from a choline-deficient mouse all gave rise to small numbers of intrahepatic nodules that subsequently were serially transplantable in the spleen and, later, subcutaneously. Of these, 6 were hepatomas and one was a reticulum-cell sarcoma. Liver from fetuses and 1-day-old mice did not undergo these changes.

- 63-121 FILTRATION OF PHENOLS FROM CIGARETTE SMOKE. (E.) Hoffmann, D. (Sloan-Kettering Inst., New York) and E. L. Wynder. J. Nat. Cancer Inst. 30(1):67-84, 1963.

The influence of various modifications of cigarette filters on phenol content of the smoke was determined under standard conditions using an Ethel Mark VI smoking machine. Increased selective adsorption for phenols was obtained when polyethylene glycol was dusted on filter fibers of cellulose secondary acetate. When cellulose secondary acetate fiber was dusted with secondary acetate power, the removal of both phenol and particulate matter was increased significantly.

Cellulose triacetate with a grain surface was superior to that with regular surfaces. Plasticizers improved phenol-adsorption capacity.

- 63-122 URBAN-RURAL DIFFERENCES IN LUNG CANCER MORTALITY RATES IN THE STATE. (E.) Gilmore, H. R., Jr. (Pa. Dept. Health, Harrisburg) and D. M. Anderson. Penn. Med. J. 66(2):43-46, 1963.

A comparison of the crude death rates for cancer of the chest cavity (1946-50) and cancer of the respiratory tract (1956-58) in 8 urban and 17 rural Pennsylvania counties showed a consistently higher mortality from respiratory cancer in the urban population, amounting to an excess urban death rate of 66-130% for men and 58-62% for women (high figures in each case for chest cavity cancer). Since the migration of older or ill individuals to the city and the factors of better diagnosis and reporting would also apply to other types of cancer, with an excess urban mortality of 5-8% for men and 15% for women, this does not account for the excess respiratory cancer mortality. If a further correction is applied for the difference in urban and rural smoking habits (13% for men and 15% for women), this still leaves 386-398 excess urban deaths per year from cancer of the chest cavity or respiratory tract (352-364 in men and 34 each in women). Some of the factors which may play a role in this discrepancy are occupational exposure to carcinogens, socioeconomic status and, especially in view of the excess mortality among women as well as men, air pollution.

- 63-123 THE EPIDEMIOLOGY OF MELANOMA. (E.) Macdonald, E. J. (U. Texas M. D. Anderson Hosp., Houston). Ann. N.Y. Acad. Sci. 100(Pt.1):4-17, 1963.

In the 3rd of a series of reports dealing with malignant melanoma, the author first discusses the age-adjusted death rate for Texas on the basis of the 1313 melanoma deaths between 1949 and 1960 (increasing from 0.975 in 1949 to 1.660 in 1956 and then leveling off) and points out that the highest incidence of melanoma on the basis of these same figures was not in the counties with the most sunshine. She then presents the results of an analysis of the 913 cases of melanoma seen between 1944 and 1960 at the University of Texas, 78 of whom were autopsied at this institution. Information is given as to the distribution of melanoma by age and sex and by stage of disease, and the type and extent of metastasis are analyzed in detail. Ten-year survival rates for pts. without metastases were 50% in males and 60% in females, compared to 5-year survival rates of 10% for males and 16% for females with metastases when first seen.

- 63-124 AN IMMUNOLOGIC UNITARIAN CONCEPT OF CANCER. (E.) Makari, J. G.

(Muhlenberg Hosp., Plainfield, N. J.). J. Am. Geriat. Soc. 11(2):167-183, 1963.

Cancer is viewed as a train of events induced by excessive stimulation of abnormal polysaccharide substances which accumulate in host tissues as a result of prolonged irritation. Chemical carcinogens, viruses, physical agents, hormones, and other agents which are now regarded as causes of cancer seem to share this common property, namely, the ability to produce endogenous formation of tumor-specific antigenic polysaccharide substances (TPS). Development of cancer is believed to take place in stages: (1) Isogenic immunity to TPS produced as a result of alteration of normal cell-wall polysaccharides by carcinogens. (2) Immunologic paralysis--due to excessive accumulation of TPS is analogous to a state of tolerance to a homograft in conditioned hosts. (3) Dormancy, in which adult nonantibody-producing cells are transformed to "embryonic" potentially competent cells as a result of alteration by TPS of the cell-stroma interaction. (4) Autonomy, in which dormant cells become immunologically competent. (5) Auto-sensitization. (6) Tumor cell formation--the result of alteration by TPS of chromosomal DNA. (7) Tumor spread--the result of introduction to a normal cell of the altered cancer DNA which by transduction takes over cell function completely. Extensive comparison is made with Green's deletion hypothesis.

63-125 THE ONCOGENIC ACTION OF BRAIN FILTRATES FROM ACUTE LEUKEMIA PATIENTS. (E.) Levina, D. M. (N. F. Gamalei Inst. Epidemiol. Microbiol., Acad. Med. Sci., Moscow) and V. A. Parnes. Vop. Onkol. (Eng.) 7(12):10-14, 1961.

Brains of pts. who had died of acute leukemia without medical treatment were made into saline homogenates and passed through a Berkefeld filter prior to use. Fresh brain filtrate (from pt. R) was injected intracerebrally (0.05 ml) into C57 BL mice (21); after 8½-20½ mo., 4 mice died of mammary carcinoma, 2 developed adenocarcinoma of the lungs (one also had a mammary gland tumor). After the same filtrate was warmed for 60-70 min at 65° C, 3/20 mice exhibited tumors (2 lung, 1 mammary). Fresh brain filtrate (from pt. T) injected i.p. (0.5 ml) into CC57 BR mice resulted in 4/19 with tumors (all lung); the same filtrate after warming (60 min. at 65° C) resulted in 1/18 mice with a tumor (lung). The same filtrates (fresh and warmed) led to no tumor development in groups of 9 and 8 CC57 W mice, resp., also injected i.p.

63-126 OBSERVATIONS ON THE INCIDENCE, BIOLOGY, AND PATHOLOGY OF SKIN CANCER AMONG FILIPINOS. (E.) Pantangco, E. E. (U. Santo Tomas, Manila, Philippines), M. Canlas, G. Basa and R. Sin. Nat. Cancer Inst. Monogr. (10): 109-125, 1963.

The 10 most common sites of cancer, which ac-

counted for 2.3% of all deaths in the 3 largest general hospitals in Manila in 1960, were the uterus, breast, oral cavity, skin, reticuloendothelial lymph nodes, colon and anal canal, stomach, liver, nasopharynx, and ovary. Incidence of skin cancer was 10-15/100,000 pts. In 330 cases of skin cancer the most commonly affected age group was from 40 to 70; sex distribution was 174 males and 156 females; epidermoid carcinoma and melanoma were more common in males while basal-cell and adnexal carcinoma were more common in females. The head and neck accounted for 67% of the 180 epidermoid carcinomas, 92.3% of the 104 basal-cell carcinomas, and 3/5 adnexal carcinomas; 27.8% of the epidermoid carcinomas and 90.2% of the melanomas were in the trunk and lower extremities. Possible suggested etiological factors included sunlight, trauma, burns, X-irradiation, chemicals, infections, dietary habits, occupational carcinogens and heredity factors, with emphasis on prolonged exposure to sunlight and chronic irritation; the low incidence of skin cancer in Chinese may indicate a genetic component.

63-127 MALIGNANT TRANSFORMATION OF MOUSE CONNECTIVE TISSUE GROWN IN DIFFUSION CHAMBERS. (E.) Shelton, E. (NCI, Bethesda), V. J. Evans and G. A. Parker. J. Nat. Cancer Inst. 30(2):377-391, 1963.

Mouse C3H fibroblasts cultivated for 23 mo. in diffusion chambers (made of lucite and membrane filter) implanted by laparotomy in isologous hosts aged 3-6 mo. produced, on i.m. or intraocular injection, transplantable sarcomas. The alteration to malignancy occurred, apparently simultaneously, both in cell populations transferred monthly and in those maintained undisturbed for 260-378 days in the same host. Thus the repeated stimulation of mitosis (on transfer) as a possible factor in the induction of malignancy may be ruled out. Cells after cultivation in chambers for over a year, and then transfer to in vitro conditions, produced tumors at about the same time as those grown continuously in the diffusion chambers. No tumors were formed on the outside of the diffusion chambers nor in the peritoneal cavity of the hosts. As for the genetic factor, peritoneal tumors are rare in the C3H strain used.

63-128 FAMILIAL AGGREGATION OF LUNG CANCER IN HUMANS. (E.) Tokuhata, G. K. (Johns Hopkins U. Sch. Hyg., Baltimore) and A. M. Lilienfeld. J. Nat. Cancer Inst. 30(2):289-311, 1963.

Among 1632 relatives of 270 lung cancer probands, 170/844 deaths were attributed to cancer (representing 20% of all deaths). Among 1542 relatives of 270 neighborhood, matched controls, 96/709 deaths were due to cancer (14% of all deaths). In the proband group, 32% of all cancer was in the respiratory system, compared to 20% in the control group. This excess lung cancer mortality

was not accounted for by age, sex, generation, and cigarette smoking factors. The familial effect was more marked among nonsmokers than among smokers. The smoking effect was more evident among control relatives than among proband relatives. The effect of the familial factor among nonsmokers was similar in both men and women. The over-all excess mortality from lung cancer for all the proband relatives was statistically significant, regardless of the history of cigarette smoking. The observed number of lung cancer deaths was nearly 4 times greater than expected among proband relatives who did not smoke cigarettes; it was about 2 times greater in those who smoked cigarettes. There was among proband relatives a substantial excess mortality due to noncancer respiratory diseases. From the totality of all results, it would appear that genetic factors may play a role in the etiology of lung cancer, together with environmental factors, such as cigarette smoking.

- 63-129 CHARACTERS OF MAMMARY TUMOURS IN BALB/c FEMALE MICE FOSTER-NURSED BY C3H AND RIII MOTHERS. (E.) Squartini, F. (Div. Cancer Res., U. Perugia, Italy), G. Rossi and I. Paoletti. *Nature* (Lond.) 197:505-506, 1963.

The characters of the mammary tumors of BALB/c mice foster-nursed from birth by RIII or C3H mice tended to become like those of the nurse donor strain. Thus, in C3H and in BALB/cfC3H mice, clinical duration was 49 and 59 days, resp.; for RIII and BALB/cfRIII, duration was 103 and 104 days, resp. Partial regressions (%) for the two pairs were 27 and 34 vs. 59 and 60; type of growth (regular: %) 64.3 and 61.5 vs. 30 and 25; morphological picture (prevalent), pure, pure vs. varied, varied

- 63-130 CYTOLOGICAL DEMONSTRATION OF THE CLONAL NATURE OF SPLEEN COLONIES DERIVED FROM TRANSPLANTED MOUSE MARROW CELLS. (E.) Becker, A. J. (Dept. Med. Biophys., U. Toronto, Ontario, Canada), E. A. McCulloch and J. E. Till. *Nature* (Lond.) 197:452-454, 1963.

Eleven days after transplantation of bone marrow from the femora of females into the spleens of irradiated mice of either sex of the same strain (Swiss), followed by further irradiation, demecolcine was injected i.p. and the recipients were killed 1 hr. afterwards. After a study of 42 discrete colonies in the spleens of 36 animals, 4 were seen to contain obviously abnormal karyotypes (cells containing 36-40 chromosomes, 1 colony had some cells with 35 or less). In these colonies, an overwhelming majority of the cells contained the same marker chromosomes. A similar study of intrasplenic colonies from the same donor marrow, but in animals only irradiated before transplantation, revealed cells exclusively with the normal female diploid complement of 40 chromosomes. It is felt the direct cytological evidence plus the indirect support provided by

the dilution and radiation-survival data would support the view that the spleen colonies are clones.

- 63-131 IMMUNOLOGICAL STUDIES AND BEHAVIOUR OF HUSBAND AND FOREIGN HOMOGRAFTS IN PATIENTS WITH CHORIONEPITHELIOMA. (E.) Robinson, E. (Dept. Oncol., Hadassah U. Hosp., Jerusalem, Israel), J. Shulman, N. Ben-Hur, H. Zuckerman and Z. Neuman. *Lancet* 1:300-302, 1963.

Each of two multiparous patients (47 and 44 yr.) with chorionepithelioma following production of a hydatidiform mole and hysterectomy (+ oophorectomy in the latter case), both of blood group B, Rh+, received homografts of split-thickness skin from their respective husbands (both of blood group A, Rh+) and from foreign donors of blood group B, Rh+. The foreign skin grafts, after initial take, were sloughed off after 14 and 7 days, while the husband homografts persisted at time of report, 3 and 2 mo. later. In each case the anti-A titer was higher after the transplant. No agglutinins against their husbands' leukocytes appeared on repeated serum examination, and in both cases the leukocyte antigens of both spouses were highly compatible (5/6 and 4/6, antileukocyte sera, resp.). In the first pt., the homografts were made while under therapy with methotrexate (315 mg in 55 days; + prednisone, 15 mg/day) and repeated 16 days after termination of drug therapy, with similar results. The findings support the hypothesis of genetic similarity between the tissues of husband and wife; this similarity may even account for the failure to reject the original chorionepithelioma. Other possible explanations considered are (1) an immune paralysis caused by the tumor, and (2) development of an immune tolerance to some of the husband's antigens by derangement of the pt.'s antibody-producing mechanism.

- 63-132 PRECANCEROUS LESIONS OF THE INTESTINE. (E.) Marozzi, G. (Surg. Clin., U. Perugia, Italy). Pp. 579-581 in *The Morphological Precursors of Cancer*. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Attention is called to the close correlation between polyposis and cancer. Their frequent co-existence in a given patient, their similar anatomical distribution, and their highly familial occurrence are striking. The frequency of polyposis in the large intestine and the high incidence of its transformation into cancer (especially where polyps are multiple and disseminated), calls for the early diagnosis of these precancerous lesions and their prompt excision, either by proctoscopic intervention or sometimes by wide intestinal excision.

- 63-133 A SYSTEMATIC APPROACH TO THE STUDY OF THE MORBID CHANGES INDUCED BY SPONTANEOUS CANCERS AND THEIR PRECURSORS IN MAN. (E.)

O'Meara, R. A. Q. (Sch. Path., U. Dublin, Trinity Coll., Ireland). Pp. 21-34 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In the histological study of tissue showing invasive growth, it was found that fibrin threads are laid down on cells as they infiltrate tissues. The fibrin which occurs in cancers has been found to be related to a very labile coagulative factor. This factor has also been found in fetal membranes and placenta, and in apparently normal adult colon but has not been found in other adult normal tissues studied. Cancer tissue (in contrast to most normal tissue) lacked fibrinolytic activity. From electrophoretic studies of the factor (which is readily diffusible) it was found that normal tissue and normal blood contain an inhibitor for the coagulative factor.

63-134 LIVER CIRRHOSIS AND LIVER CANCER. (E.) Korpásky, B. (Dept. Path. Anat. and Pathohistol. U. Med. Sch., Szeged, Hungary). Pp. 177-189 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

During a 15-year period, in a survey of necropsied pts., 99 cases of hepatic cirrhosis and 13 cases of primary hepatic carcinoma were encountered. Frequently seen in posthepatic cirrhotic livers were irregularly arranged groups of highly abnormal cells with enlarged hyperchromatic nuclei and conspicuous nucleoli (often multinucleated) and transformed epithelial cells which were suggestive of incipient carcinomas or at least precancerous lesions. The highest incidence of primary liver carcinoma was in association with posthepatic cirrhosis (7/39, 18%), lowest was in association with nutritional cirrhosis (1/35, 2.8%). After treatment of rats with tannic acid (s.c.) + 2-acetylaminofluorene (AAF; in the diet) for 90-180 days, 11/18 showed advanced cirrhosis and 17/18 both cirrhosis and + tumor. Of 5 rats treated only with AAF, all showed early cirrhosis, 1 showed cirrhosis and tumor. This experiment suggests that liver cirrhosis is an important promoting factor in experimental hepatocarcinogenesis.

63-135 LYMPHOCYTE PRODUCTION AND DIFFERENTIATION IN THE PRELEUKAEMIC MOUSE THYMUS. (E.) Metcalf, D. (Roy. Melbourne Hosp., Australia) and K. Nakamura. Pp. 269-278 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In a comparative survey of AKR and C3H mice in the 0-6 mo. age period, it was found that while body weights were identical, the thymuses of AKR mice at all ages after 1 wk. were 2-3 times heavier than those of corresponding C3H mice. No significant strain differences were found in the weights of the other lymphoid organs examined--subcutaneous lymph nodes, mesenteric node and spleen. The mitotic index of thymic lymphoid

cells in AKR mice was substantially higher than in those of C3H mice. Commencing at 6 mo. there was an increase in the primitive cell content of AKR thymuses. This preceded the development of neoplastic cells in these thymuses, and apparently represented a partial failure of differentiation. While its significance is not known, between the ages of 6-8 mo., there was a decrease in size of the cortex and an increase in the size of the medulla in AKR thymuses. Lymphoma tissue was composed of a high percentage of primitive cells with a low mitotic index.

63-136 ON THE LEUKEMOGENIC EFFECT OF HUMAN SPERM. (E.) Baló, J. (Dept. Path. Anat., Med. U., Budapest, Hungary), E. Juhász and G. Kendrey. Pp. 279-282 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Human sperm was injected i.p. into 123 white mice of both sexes, 6-8 times at intervals of 2-3 days. Doses of 0.2 ml were tolerated but higher doses were usually followed by hemorrhages. Of 48 mice that survived for at least 8 mo.-1 yr., leukemia developed in 11 and pulmonary adenomas in one. Leukemia occurred in only 1/50 control mice. As to type, 10/11 cases in the treated group and the 1 in the control group proved to be lymphatic leukemia; the 11th case in the treated group was myeloid leukemia.

63-137 THE RESPIRATORY EPITHELIUM OF PATIENTS WITH LUNG CANCER. (E.) Carnes, W. H. (Dept. Path., U. Utah Coll. Med., Salt Lake City). Pp. 625-634 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In a collaborative study to determine the lesions associated with lung cancer, sections from nine sites in the trachea and bronchi of 119 cases of lung cancer were compared to those of 238 controls closely matched to them by age, sex, race and date of death. Hyperplasia of the respiratory epithelium without distinct metaplasia occurred with such high frequency in all segments of the respiratory tree that it cannot be regarded as a precancerous lesion. Metaplasia of all types was only slightly more common in both tracheas and bronchi of lung cancer cases than in the controls. While the transitional, squamous and regenerating types of metaplasia showed normal incidences, the type known as atypical metaplasia had a substantially higher incidence in the cancer cases and with one exception was confined to the bronchi. Carcinoma *in situ* was diagnosed only in the lung cancer group. The coincidence of atypical metaplasia and carcinoma *in situ* was far greater than the incidence of either one in the cases of lung cancer in general and was high enough to support the contention that it may be a precancerous lesion.

- 63-138 STRUCTURAL AND HISTOCHEMICAL ASPECTS OF PRECANCEROUS CHANGE IN THE BRONCHIAL EPITHELIUM. (E.) Cunningham, G. J. (Roy. Coll. Surg. Eng., London, England). Pp. 613-620 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In a study of variations of the normal bronchial epithelium, it was found that the nuclei in basal cell hyperplasia could be either pale-staining or dark-staining. Nuclear phospholipid was absent in fully differentiated squamous metaplasia but present in the deeper layers. The nuclei of cells in areas of basal cell hyperplasia, when stained in vitro with benzpyrene, showed marked uptake of the carcinogen. It is suggested that phospholipid may play a part in the selective absorption of carcinogenic substances.

- 63-139 RELATIONS BETWEEN CYSTIC DISEASE AND BREAST CANCER. (E.) Bucalossi, P. (Nat. Cancer Inst., Milan, Italy) and U. Veronesi. Pp. 389-394 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In 761 cases of cystic mammary gland disease seen between 1938 and 1958, 728 were treated surgically (637 by resection and 91 by mastectomy). Age at time of admission ranged from 15 to 89 yr., with 56.8% between 40 and 49 yr. From actuarial analysis of person-years at risk, the expected cases of mammary cancer (based on U.S. data) among such a group was 5.09. Observed incidence (2-14 yr. after 1st admission) was 12. It is suggested that this increased breast cancer incidence (2.5 x expected) in women with cystic disease may be correlated with their surgical treatment, possibly because of the high hormone concentration in the remaining breast tissue. A "majority" of pts. with cystic disease who developed mammary cancer had undergone previous extensive breast resection: 2 had monolateral total mastectomy. Therefore surgery for cystic disease should be approached with more caution. Among 63 cases of cystic disease treated with androgens there was

a higher rate of recurrence (compared to the remaining cases) during 3-21 yr. of follow-up: 3 breast cancers 6, 10, and 13 yr. after hormone therapy. Since intracystic and intraductal proliferation was "frequently" observed in breast tissue removed after testosterone therapy, it was concluded that androgen therapy should be discarded in the treatment of cystic disease.

- 63-140 SOME EPIDEMIOLOGICAL ASPECTS OF CANCER OF THE PROSTATE. (E.) King, H. (NCI, Bethesda), E. Diamond and A. M. Lilienfeld. J. Chronic Dis. 16(1):117-153, 1963.

In the hope of obtaining some indications as to the etiology of prostate carcinoma and some guidelines for future statistical research, the authors present an extensive review of the epidemiological literature in this field and an analysis of data from 33 cities in the USA regarding the trends in morbidity and mortality due to prostate cancer and the distribution by such characteristics as age, race, geographical area, nativity, religion, marital status, socioeconomic standing and familial aggregation. Some of the findings are: a continuing increase in mortality among the non-white population, an over-all mortality rate varying from 22.3/100,000 in the USA (non-white) to only 1.1/100,000 in Japan, a geometrical increase from the age of 40-50 upwards, a low frequency among Orientals and Indians but high among Negroes, a higher frequency in the northern USA than in the south, but little difference between urban and rural areas, a lower frequency among foreign-born whites than among native Americans, a low frequency among Jews and high frequency among Protestants, a higher frequency among married or divorced than among single persons, and a higher frequency among married with children, generally no socioeconomic gradient, but more frequent among professionals than among workers, and a high frequency among male relatives of prostate cancer decedents. The authors conclude that both genetic and sociocultural factors (such as sexual behavior) probably play a role. (75 references)

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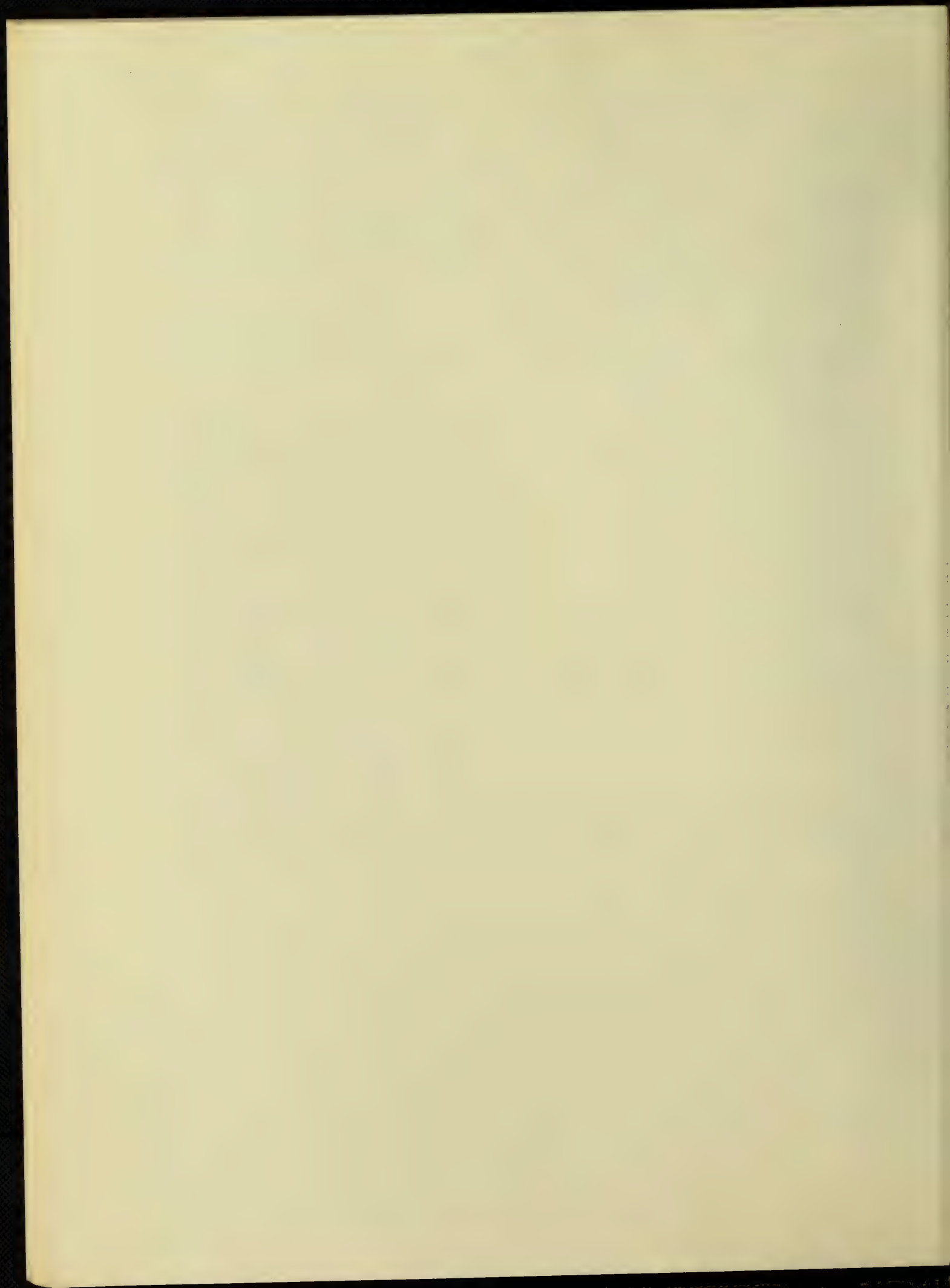
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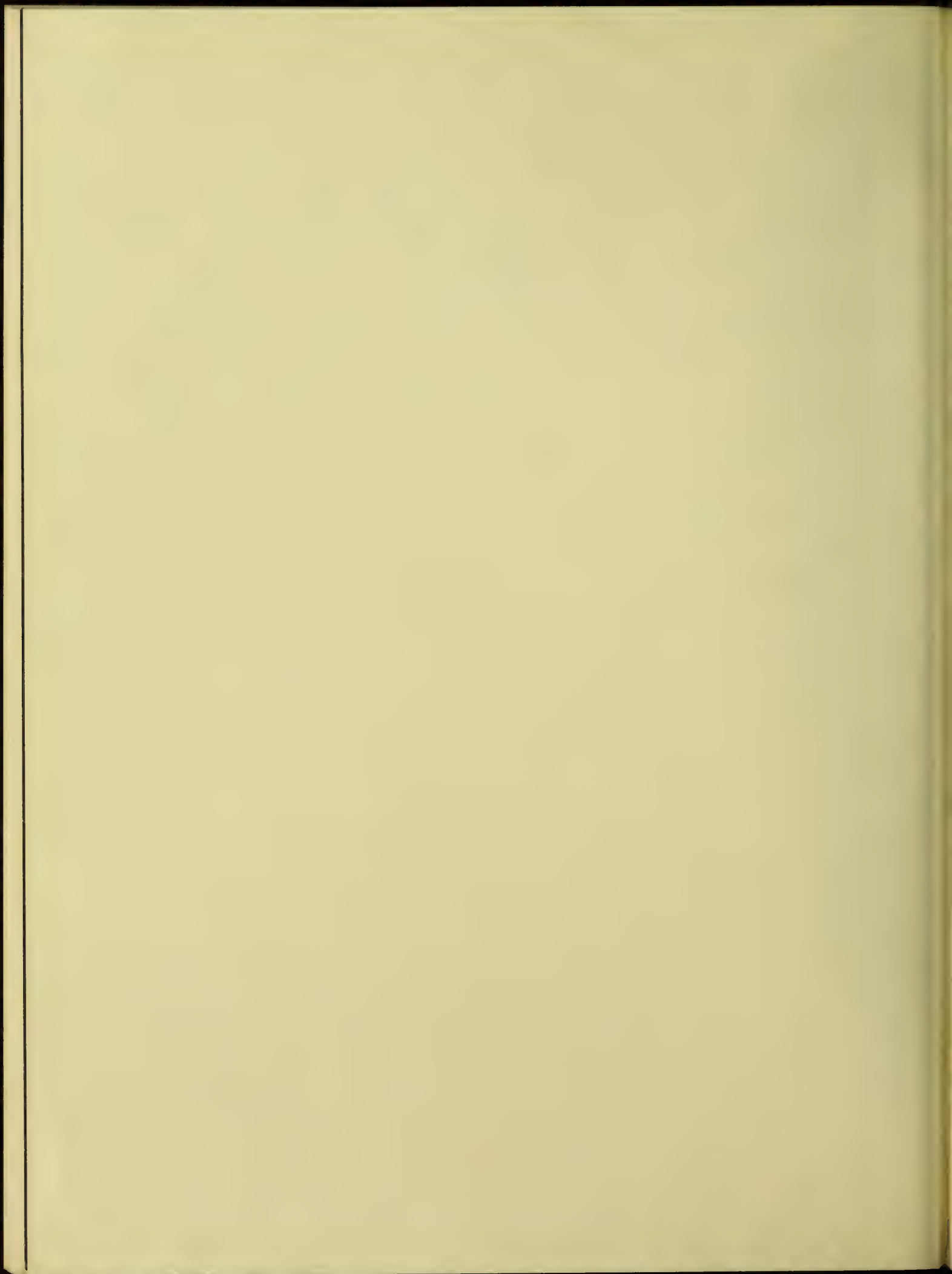
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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NIH	National Institutes of Health, USA
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	QO ₂	oxygen quotient
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FFU	focus forming unit	pt.(s)	patient(s)
g.i.	gastrointestinal	RBC	red blood cells (erythrocytes)
g	gram(s)	RES	reticuloendothelial system
μg	microgram(s)	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
i.a.	intra-arterial	RNase	ribonuclease
LD ₅₀	median infectious dose	soln.	solution
inj.	injected, injection(s)	s.c.	subcutaneous
inoc.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
i.p.	intraperitoneal	x	times (e.g. x 3/wk.)
I.U.	international unit(s)	U	unit
i.v.	intravenous	UV	ultraviolet
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose	VA	Veterans Administration
M	molar, mole(s)	wt.	weight
mM	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
μM	micromole(s)	yr.	year(s)
max.	maximum		

LANGUAGE ABBREVIATIONS

Af.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukranian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

63-141 CAUSES OF CONGENITAL MALFORMATIONS.
(Fr.) Tuchmann-Duplessis, H. Rev. Epide-
miol. Hyg. Pub. Sanit. 12:14-16, 1962.

The frequency of congenital malformations estimated at 2 to 3% per annum, on a global scale, would represent 600,000 abnormal children a year. After an enumeration of some congenital disorders genetically transmitted and induced by chromosomal aberrations, external sources of congenital malformations are considered. Since first it was learned that in swine a vitamin A deficiency in the mother may induce microphthalmia, hare-lip, etc. in the offspring, almost 400 teratogenic factors have been discovered thus far. Known teratogenic factors discussed include irradiation; hypoxia; avitaminosis and hypervitaminosis; infection; chemical agents (including hormones); hypoglycemics; antibiotics; and neuroleptics. The placental barrier does not wholly protect the fetus from external injurious substances. Many malformations have been ascribed to folic acid deficiency secondary to the use of antagonists like folic acid and 10-methyl folic acid.

63-142 RECENT FINDINGS IN CANCER RESEARCH.
(Ger.) Seelich, F. (Austrian Inst. Cancer Res., Linz, Austria). Wien. Med. Wschr. 3(2):43-48, 1963.

The problems of malignant transformation and its early detection and control are discussed on the basis of recent data in the literature. The author discusses the uncontrolled proliferation of neoplastic cells, ascribed to the absence of receptors to "steering" mechanisms, and their loss of organ-specific antigens. The defect responsible for the transformation of a normal cell to a malignant one is attributed to a structural modification of cytoplasmic molecules involved in reduplication, rather than to a chromosomal defect or classic mutation. After transplantation of a completely inert foil, cell change occurs in the blood-vessel-poor region of connective tissue close to the foreign body; however, the same material in powder form or with any perforations does not produce sarcoma. Another nonspecific factor is radiation. In contrast, the effect of chemical carcinogens is bound to very specific molecular structures, slight changes of which cause loss of carcinogenicity. The extent to which substances shown to be carcinogenic in animals are involved in human cancer can be determined only by careful statistical studies, but the role of smoking in promoting cancer of the lungs can be regarded as proven. Also considered proven is the responsibility of smoked flesh and fish for the high incidence of esophageal carcinoma in certain populations and probably for the higher incidence of gastric carcinoma in men than in women. Endogenous--especially hormonal--factors are also discussed, as is the hypothesis of the viral etiology of human neoplasms, most tenable in the case of leukemia. In

the author's opinion, the most hopeful avenues for further discovery are research on the mechanisms directing cell multiplication and differentiation, as well as virology and the study of immune reactions. (65 references)

63-143 THE VIRAL ETIOLOGY OF LEUKEMIA. (Ger.) Georgii, A. (Path. Inst., U. Munich, Germany). Blut 9(8):470-487, 1962.

In an exhaustive survey of the literature, the author discusses the various types of virus-induced mouse leukemia (such as Friend, Moloney), polyoma virus, and the agent of parotid tumor. It is remarkable that leukemia is not caused by polyoma virus, although it has been isolated from virus-induced and virus containing leukemias. The reason could be: 1. that the leukemia and polyoma agents are not identical, and only the latter could be cultivated *in vitro*; 2. that the manifestation of leukemia is masked, because of the more rapidly formed tumors which cause death. Despite the negative and contradictory evidence for the viral etiology of human leukemias, it can be regarded as probable that viruses represent one of the many causal factors responsible for their development. All findings confirm the viral origin of specific leukemias and tumors in mice and other rodents; leukemia viruses could be found in different tissues. Viruses are often carried alone, latent or masked, in tissue, and because of their wide distribution their contagious quality is considerably increased. The morphological study showed 6-7 different virus types which induce lymphatic, myeloid, reticulum-cell or monocytic leukemia, as well as parotid or multiple tumors (polyoma). (224 references)

63-144 BASIC MECHANISMS IN THE BIOLOGY OF ANIMAL VIRUSES. (E.) Dulbecco, R. (Calif. Inst. Tech., Pasadena). Pp. 519-525 in Basic Mechanisms in Animal Virus Biology. V. 27 in Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

In this concluding address of the symposium, one problem examined is the structure of the virus and its biological significance: included are methods of viral replication and influence of environmental factors. One change attributable to virus action is the probable incorporation of a new component into the cell surface, which initiates the physiologic alterations that may stimulate cell growth. Others are the cytotoxic suppression, by a virus, of cell messenger RNA synthesis, and the alteration of some genetic cell component when it is transformed by viral action, with the disappearance of the causative DNA-containing virus. Factors in tumor induction that are touched upon include the virus itself, the physiologic alteration of normal cells, and the antigenic changes that characterize induced (but not spontaneous) tumors. (9 references)

63-145 RELATIONSHIP OF COMPONENTS OF PAPILLOMA VIRUS TO PAPILLOMA AND CARCINOMA CELLS.

(E.) Ito, Y. (Dept. Microbiol., U. Wash., Seattle). Pp. 387-394 In Basic Mechanisms In Animal Virus Biology. V. 27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

This discussion of the interactions of viral components with their host cells (which includes some of the author's own findings), points out that the nucleic acid moiety of Shope papilloma virus possesses both infectious and tumorigenic properties. These findings indicate too that the major role in the neoplastic induction of Shope papillomatosis is played by the DNA extracted from the virus, and that this DNA extract, even when partially heat-denatured, retained both its biological activity, i.e. its tissue-specific tumorigenesis, and its species specificity. It was also demonstrated that this incomplete viral DNA could cause the synthesis (in suitable host tissues) of complete, intact, infectious virus particles. The 'masking' phenomenon of virus particles is discussed, as well as some properties of induced malignancies. (43 references)

63-146 RELATION OF BENIGN AND MALIGNANT EPIDERMAL HYPERPLASIA IN MOUSE. (E.)

Setälä, K. (Dept. Path., U. Helsinki, Finland). Pp. 529-540 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Following a brief review of the literature on the morphological relationship between cancer and its precursors (with emphasis on epithelial hyperplasia in the mouse), the author details some of the experimental principles on which his own work is based: the concept of growth (the distinction between cellular proliferation and differentiation); the special characteristics of mouse epidermis as a target tissue for tumor formation; the differentiation between benign and malignant responses in the skin; the varying susceptibility of mouse strains; and the relationship between the experimental method and the biological response produced. Benign epidermal hyperplasia produced by tumor-promoting agents can be looked upon not only as a protective response but also as a precursor of skin cancer, while malignant hyperplasia produced by carcinogens is characterized by a delayed and misdirected maturation of the epidermal cells. The average lifetime of a carcinogen-damaged epidermal cell is significantly longer, not shorter, than that of cells in benign hyperplasia, or even normal cells. Thus, benign epidermal hyperplasia is not part of the carcinogenic process as such, but merely provides the conditions for the manifestation of carcinogenesis initiated by the appropriate stimulus. The hereditary inhibition of epidermal maturation produced by a carcinogen leads to a deficiency of mature cells which may activate the epidermis to reparative proliferation.

63-147 PRECANCEROUS LESIONS OF THE RAT LIVER.

(E.) Maisin, J. (Inst. Cancer, Catholic U. Sch. Med., Louvain, Belgium), P. Maldague and L. Deckers-Passau. Pp. 167-176 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Extensive histological studies of the liver and measurements of the activity of hepatic acid phosphatase, β -glucuronidase, cathepsin, acid RNase and acid DNase in rats fed p-dimethylaminoazobenzene or 2-acetylaminofluorene plus a basic rice diet, with or without the addition of 40% defatted liver pulp (which prevents the induction of hepatic carcinoma), showed a marked decrease in acid phosphatase in all cases (apparently unrelated to tumor induction) and increases in cathepsin and acid RNase and DNase activity. These changes seemed to parallel the development of precancerous regenerative foci in rats not given defatted liver pulp. Histological lesions due to dimethylaminoazobenzene first appeared after about 30 days and consisted of small groups of cells with elongated nuclei, dusty chromatin, and scarce and basophilic protoplasm, which usually appeared in the vicinity of the smaller divisions of biliary ducts and in the vicinity of the portal spaces. These regenerative foci became larger and more numerous, eventually showed differentiation into either bile ducts or hepatic cells. In 50-60 days, another lesion appeared which exhibited pyknotic nuclei, giant nuclei, binucleated cells and dwarf cells with micronuclei among the hepatic lobules; after 70 days, zones of vacuolar necrosis became more frequent, and the regenerative foci may develop into cystic cholangiomata, which may or may not eventually become malignant. Since typical cirrhosis is rare, cirrhosis is looked upon as a process which may parallel carcinogenesis but does not necessarily precede cancer. Addition of defatted liver pulp to the diet prevented the development of the regenerative foci described above, but not common lesions such as pyknosis and vacuolar necrosis.

63-148 MORPHOGENESIS OF CANCER OF THE LIVER.

(E.) Symeonidis, A. (Dept. Path., Aristotelian U., Sch. Med., Thessalonica, Greece). Pp. 203-217 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Histological studies of the liver 1-28 days after ligation or excision of the common bile duct in adult male Osborne-Mendel rats showed increasing transformation of liver cells into bile duct cells, beginning at the periphery of the lobe and becoming apparent in about 7 days; initial anisocytosis and anisokaryosis developed into marked hyperplasia and eventually into extreme hepatic necrosis. Following simple ligation, however, recanalization generally occurred and the pathological changes taking place during the first 2 wk. were found to be completely reversible. In other experiments, 209 adult, male rats were fed 3'-methyl-4-dimethylaminoazobenzene for periods of 4-17 wk., after

which some were immediately sacrificed and some were fed a regular diet for 9 wk. before sacrifice and histological study of the liver. Hepatic tumors developed in none of 63 rats fed the azo dye for 4 wk.; in 1/49 fed the dye for 8 wk.; and in all 107 fed the dye for 12-17 wk. Microscopic study of the livers of rats killed during administration of the carcinogen revealed a very wide variety of greatly varying differing cellular forms resulting from the interplay of regressive and progressive changes. The most characteristic neoplastic changes were "chromolysis" (loss of chromophilic substance of the liver cells), proceeding from the center of the lobe outwards; transformation of liver cells into bile duct cells; and later cholangiofibrosis. All of these conditions in rats fed dye 4-8 wk. were reversible when they were placed on a normal diet. In rats fed dye for 12 wk., these regressive changes were accompanied by progressive liver changes, with the formation of giant polymorphic cells and occasional nests of hematopoietic tissue between the newly formed liver cords. Under the prolonged influence of the carcinogen for several successive cell generations, minute foci of anaplastic liver cells appeared, forming irregular cords and duct-like formations; these anaplastic cells were no longer reversible when the rats were placed on a normal diet. Some of these areas grew into tiny tumors which thus may be considered the true beginning of an hepatic neoplasm.

63-149 THE PRECANCEROUS LESIONS ASSOCIATED WITH PRIMARY CARCINOMA OF THE LIVER. (E.) Berman, C. (Durban Roodepoort Deep Mine Hosp., Transvaal, South Africa). Pp. 229-249 in The Morphological Precursors of Cancer. Severi, (Ed.). Perugia, Div. Cancer Res., 1962.

On the basis of his own observations on carcinoma of the liver in the African Bantu, and a review of the literature on the etiology of hepatoma in man and animals, the author discusses the role of some of the pathological changes which may predispose the liver to the later development of frank neoplasm; these include cirrhosis of the liver, infestation with liver flukes, hydatid cysts and schistosomiasis, hemochromatosis and liver damage due to chronic malnutrition or alcoholism. These conditions are illustrated by a large number of histological sections. Not one of the conditions cited is invariably present in every case; nor are they common to all communities known for their high incidence of liver disease. The author concludes that prolonged cyclical dietary inadequacy may influence the development of fibrotic and other morphological precursors of liver cancer, making the livers more susceptible to hepatotoxic and carcinogenic agents which may be present in the diet. (79 references)

63-150 THE DUAL FUNCTION OF HORMONES IN MAMMARY CARCINOGENESIS: A WORKING HYPOTHESIS. (E.) Dao, T. L. (Roswell Park

Mem. Inst., Buffalo). Pp. 231-242 in On Cancer and Hormones: Essays in Experimental Biology. Chicago, U. Chicago Press, 1962. \$8.50

Based on a two-stage process of tumor initiation by a carcinogen and its promotion by a cocarcinogen inducing hyperplasia, the hypothesis is proposed that steroid hormones may act both as initiator and promoter of mammary tumors. The initial event, it is suggested, may be an interaction between a carcinogen (a polycyclic hydrocarbon or an ovarian hormone itself) and a cellular constituent (cytoplasmic RNA or chromosomal DNA) which alters cell behavior. This interaction is made possible through an alteration (increase) in cell membrane permeability, brought about by steroid hormones which may form links with protein receptors at the cell surface; or, these ovarian hormones may so activate the protein receptors in the cell that they are enabled to interact with hydrocarbons or hormone metabolites, to form a complex which changes cell behavior (mutation?). This change probably occurs in the RNA of the cytoplasmic microsomes. The proposed hypothesis is based on the findings of experiments (published elsewhere) dealing with the effects of ovarian transplantation, excision, and grafting on the 20-methylcholanthrene induction of mammary gland tumors of rats. (25 references)

63-151 VIRUS VACCINES, CELL CULTURES AND CANCER: SOME SIGNIFICANT INTERRELATIONSHIPS. (Ger.) Brand, G. (Dept. Microbiol., U. Minn. Med. Sch., Minneapolis). Fortschr. Med. 81(2):65-69, 1963.

In a broad review based mainly on the literature and partly on his own work, the author points out the value of cell cultures in virology, but then emphasizes the similarities between continuously transplantable cell cultures and malignant cells and the consequent danger that a virus vaccine produced in such continuous cell cultures may contain carcinogenic factors; this danger persists even when non-human cells are used, due to the possible loss of species specificity following cell transformation. The establishment of continuous cell cultures, evolution and clone variation in such cultures, and the morphological, karyological, immunological and biochemical changes taking place during cell transformation are discussed in detail, with emphasis on chromosome changes during transformation and establishment of continuous cell cultures. After pointing out the difficulty of reproducing cell transformation and the usual stability of immunological species specificity in cell cultures, the author concludes that cell transformation is not a true biological phenomenon but is the result of contamination with extraneous cells. The questionable homogeneity of many continuously transplantable cell lines by no means, however, lessens the danger of using such contaminated lines for the preparation of virus vaccines. (2 references; another published work is referred to for other (287) references.)

- 63-152 CARCINOGEN-INDUCED MELANOTIC TUMORS IN THE SYRIAN HAMSTER. (E.) Rappaport, H. (Div. Oncol., Chicago Med. Sch., Ill.), T. Nakai, P. Shubik and H. Swift. Ann. N. Y. Acad. Sci. 100(Pt.1):279-296, 1963.

The authors summarize their previously published experiences with the melanotic tumors induced in the skin of the Syrian white or golden hamster by topical application of 9,10-dimethyl-1,2-benzanthracene (as little as 50 µg). The sequence of events following application of the carcinogen is described as a hyperplastic response manifested by a perifollicular proliferation of dermal melanocytes, a neoplastic response manifested by multiple melanotic tumors composed of dendritic melanocytes, and a melanogenetic response in the white hamster manifested by the conversion of dopa-negative melanocytes into melanin-forming types. These neoplasms are transplantable but not malignant, and resemble the cellular blue nevi of man; they are different from the spontaneous malignant melanomas of the Syrian hamster (which cannot be produced by carcinogens); these benign tumors, however, are not produced by any other type of carcinogen except by parenterally administered urethan. The authors then discuss some of the theoretical questions raised by these observations, dealing either with the biological features of this association between carcinogenesis and melanogenesis, or with the distinctive morphology of these tumors. The difference in response between various laboratory animals is emphasized and explained on the basis of anatomical differences, such as the perifollicular network of melanocytes seen in the hamster but not in the rabbit or mouse. Finally, the neurofibroma-like structure of the tumors is described in more detail, with suggested histogenetic interpretations, and some of the differences between the melanocyte systems of white and golden hamsters are pointed out.

- 63-153 NEW DIMENSIONS IN CANCER RESEARCH. (E.) Shimkin, M. B. (NCI, Bethesda). Public Health Rep. 78(3):195-206, 1963.

In a broad review of the literature, the author discusses two of the principal new trends in cancer research, one dealing with the global distribution and incidence of some neoplastic diseases and the other with some of the recent advances in virus research pertaining to cancer. Particular attention is drawn to the incidence of cancer of the stomach, breast, lungs, uterine cervix and liver, and to some of the etiological conclusions which may be drawn from this type of information. Cancer in animals is also mentioned; also treated is the role of viruses in the transmission of dog sarcoma, mouse mammary carcinoma and murine leukemia (polyoma virus). The author expresses confidence that a role for viruses will also be demonstrated in human neoplasms. (30 references)

- 63-154 THE RELATIONSHIP BETWEEN BENIGN BREAST DISEASE AND BREAST CANCER. (E.) Lewison, E. F. (Johns Hopkins Hosp., Baltimore). Pp. 405-410 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In the author's own series of chronic mastitis pts. traced successfully for 1-25 yr., breast cancer incidence was 2.6 to 3.6 times the "normal" expected frequency in women of a similar age range followed over a comparable length of time. Of 451 treated by surgery (mostly by local excision) 385 (85%) were traced, and 7/385 developed breast cancer (1.8%) (4/7 in the contralateral breast). A relationship does exist between breast cancer and chronic cystic mastitis, but its exact nature is not known. Both are stimulated by estrogen, and may be partly hormone-dependent. Histopathologic studies suggest that cystic mastitis may be a precursor to cancer, and some pathologists claim to have seen the transition between benign and malignant breast disease. Also, latent cystic mastitis is frequently found in breasts removed for cancer. However, it is also commonly found at autopsy in otherwise normal women.

- 63-155 HOST FACTORS IN NEOPLASTIC DISEASE: A REVIEW OF CURRENT CONCEPTS AND TRENDS IN CANCER RESEARCH. PART TWO: THE RETICULO-ENDOTHELIAL SYSTEM. (E.) Stern, K. (Dept. Path., U. Illinois Coll. Med., Chicago). Hebrew Med. J. 2:300-280, 1962.

In a continuation of a previous review, the author discusses the role of the reticuloendothelial system (RES) in resistance to cancer, with particular reference to recent work on the relationship between RE activity and carcinogenesis in experimental animals, changes in the RES of the tumor-bearing host, and the effect of stimulation of the RES on tumor growth. A section dealing generally with growth-controlling factors discusses the effect of the presence of cancer on non-neoplastic growth in the host, the effect of non-neoplastic growth processes or growth factors on tumor growth, and the importance of growth-controlling factors in carcinogenesis. (82 references)

- 63-156 HAIR GROWTH CYCLES AND SKIN NEOPLASIA. (E.) Argyris, T. S. (Dept. Zool., Syracuse U., New York). Nat. Cancer Inst. Monog (10):33-41, 1963.

As reported in the recent literature, in rabbits application of 9,10-dimethyl-1,2-benzanthracene (DMBA) during the resting phase of the hair growth cycle produced benign, self-healing hair follicle tumors; applied during active growth, papillomas were formed. Shope papilloma virus induced more tumors when applied during the growing phase. In mice, on the contrary, even a single DMBA application induced more tumors in skin in the resting

phase. After tumor appearance, however, a wave of hair growth seemed to stimulate tumor growth in the same skin area. The cause of the greater sensitivity of resting skin to carcinogens (20-methylcholanthrene or DMBA), and its mechanism, are not known. When an initiating dose of DMBA was employed on resting mouse skin, followed by croton oil, no more tumors developed than when growing skin was treated in the same manner. (28 references)

63-157 PREMALIGNANT CONDITIONS IN BREAST CARCINOMA. (E.) Dawson, E. K. (U. Path. Dept., Forrest Road Lab., Edinburgh, Scotland). Pp. 383-388 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Univ. Cancer Res., 1962.

Breast tissue epithelial proliferation is either adenosis or epitheliosis in type. Epithelial adenosis is physiologic in structure and remains benign. Epitheliosis, which lines or fills gland structures with its proliferation, originating primarily in the ducts, may later form benign cysts, with cell degeneration; if the cysts remain a viable cell lining, they may progress to malignant, usually papillomatous, epitheliosis. Malignant cells may be large, round, pleomorphic, with some mitotic activity and loss of polarity, but such alterations may not show as a sharply distinct tissue change. The transition to malignancy may be very gradual, with preoperative histories of 5-40 yr. Presarcomatous changes, more readily recognizable, originate from fibroadenomas, with progressive cellularity of the stroma and eventual epithelial destruction. Malignant tissue is usually recognizable, but interpretation of borderline hyperplasia is difficult. (3 references)

63-158 PREMALIGNANT CHANGES OF THE BREAST. (E.) Scarff, R. W. (Middlesex Hosp., London). Pp. 417-421 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Univ. Cancer Res., 1962.

Most of those breast lesions which consist of epithelial overgrowth, usually associated with some endocrine dysfunction, heretofore regarded as precancerous, are in fact benign. Such conditions are pink epithelium, simple cyst adenosis, and solitary papilloma. Opinion is divided as to the malignant or benign nature of multiple papillomatosis. Solid epitheliosis, with its rapid, irregular, atypical growth, is the type of proliferation most likely to progress to malignancy. As regards male lesions, of 41 male breasts removed for chronic mastitis (in an old series of cases), only 3 showed a dangerous degree of hyperplasia, and 2 of these were workers with diethylstilbestrol. These findings favor the current practice, where any lump (except a simple cyst) is excised from the breast for histologic study. It is doubtful whether any truly precancerous lesion can be recognized histologically. Any

lesion which can be so recognized probably has already crossed the border of malignancy. (7 references)

63-159 SOME ASPECTS OF THE CHEMISTRY OF TOBACCO SMOKE. (E.) Van Duuren, B. L. Pp. 33-47 in Tobacco and Health. James, G. and T. Rosenthal (Eds.). Springfield, Charles C. Thomas, 1962.

In a review dealing mainly with some of the recent work carried out in his own laboratory on the content of possible carcinogens or cocarcinogens in tobacco smoke, the author briefly reports chromatographic studies which revealed the presence of 23 tetracyclic or higher polynuclear aromatic compounds, including 19 hydrocarbons, 1 oxygen heterocyclic and 3 nitrogen heterocyclics; of these, 10 were found to have carcinogenic activity. The conditions for the formation of the 2 carcinogenic dibenzacridines (pyrolysis of pyridine or nicotine at 750°C) and for the aromatization of sterols are discussed. Since these compounds do not account for the apparent biological activity of cigarette smoke, other possible carcinogens (diketene from the pyrolysis of acetone, olefinic hydroperoxides from the ozonization of conjugated olefins) and cocarcinogens (substituted phenols, long-chain fatty acids) are discussed. Finally, the author suggests that selective filtration of cigarette smoke and the modification of the pyrolytic process by additives are 2 possible ways of decreasing the dangers of smoking. (34 references)

63-160 HORMONES AND CANCER. THE RESULTS OF EXPERIMENTAL STUDIES. (Ger.) Mühlbock, O. (Netherlands Cancer Inst., Amsterdam). Helv. Med. Acta 29(5-6):437-444, 1962.

A review of some of the recent advances in the understanding of the relationships between cancer and hormones, both as inducing agents and as modifiers of tumor development. The relationships between host environment and the response to hormones are illustrated by an experiment in which 2 groups of inbred mice were given estrone for 1 yr., either (a) continuously or (b) 5 days' treatment at double dosage, followed by 5 days' rest. At the end of the yr., pituitary tumors were induced in 85% and 5%, resp. In castrated inbred mice, similar interrupted estrogen therapy produced a very low incidence of mammary tumors; after continuous treatment, a high incidence. As regards the effects of hormones on already established tumors, only hormone-induced tumors seem to regress on withdrawal of hormones later in their development. As shown by thyroid tumors, however, the absence of inducing hormone, while inhibiting tumor growth, does not usually lead to complete regression, since the tumor cells eventually become autonomous. Progression from hormone-dependence to autonomy is irreversible. It is an example of the adaptability of malignant cells. This adaptability also accounts for the resumption of tumor growth following a temporary check with chemotherapy, contrasexual hormone administration, or other measures.

The mechanism of hormone action is also discussed, it being assumed that a direct action on the tumor cell is most likely, probably in the sense of a modification in either the metabolic enzyme systems of the cell or the physicochemical properties of the cell surface. See also CRA 1(1):#8, 1963. (7 references)

- 63-161 ENDOCRINE DEPENDENCE IN EXPERIMENTAL TESTICULAR TUMORIGENESIS AND TUMOR GROWTH. (E.) Gardner, W. U. (New Haven, Conn.) Pp. 391-411 in Biological Interactions in Normal and Neoplastic Growth. Brennan, M. J. and W. L. Simpson (Eds.). Boston, Little, Brown and Co., 1962.

In a detailed review of his own work and that of others, the author discusses the etiology and growth requirements of testicular interstitial cell tumors which sometimes develop in BALB/c or Strong A mice, but usually only after prolonged exposure to estrogens, especially synthetic estrogens such as triphenylethylene or tri-p-anisyl-chloroethylene. The tendency to develop such tumors is transmitted by both males and females in a dominant or semi-dominant way, and tumor development is favored by cryptorchidism and probably by the action of pituitary hormones. Some of the irreversible early changes (interstitial hypertrophy, cytoplasmic vacuolation and intertubular brown cells) which seem to presage the development of tumor nodules and anaplastic cells are described in detail. It has been shown that the genetic susceptibility to these tumors lies in the testis itself and not in the general metabolism of the animal. After withdrawal of estrogen, some tumors regress while others continue to grow, a similar variability being shown in transplantation experiments into intact, hypophysectomized and/or estrogen-treated male or female hosts. Hormone production by the interstitial cell tumors is also quite variable both as to type and quantity. (38 references)

- 63-162 SEARCH FOR THE ESSENTIAL FACTORS OF CARCINOGENESIS. (E.) Wakonig-Vaartaja, R. (U. Adelaide, S. Australia). Ann. N.Y. Acad. Sci. 105(Pt. 1):3-24, 1963.

In an extensive review of the literature on the contradictory theories pertaining to the etiology of cancer, the author emphasizes that the neoplastic transformation is a complex process which cannot be explained satisfactorily by any one cause. The genetic nature of neoplasia, the role of viruses, the initiation and promotion of neoplasms, the question of dormant tumor cells, the relationship between neoplasia and the changes seen in tissue culture, homeostatic control mechanisms in the normal organism, and the occurrence of epiphenomena (secondary changes) in neoplasms are discussed, and a general theory is propounded based on the idea that cancer is a heritable disturbance in the controlling mechanisms which maintain homeostasis in cell division

and tissue growth, i.e. a mutational change in DNA or RNA molecules or other unknown genetic determinants. A wide variety of such mutations may result from a variety of noxious influences, including viruses, toxins and radiations, and may result in a variety of neoplastic diseases. (102 references)

- 63-163 THE MAMMALIAN ONCOGENIC VIRUSES. (E.) Stewart, S. E. (NIH, Bethesda). J. Am. Med. Women's Assn. 18(2):129-136, 1963.

In this review is discussed the specificity of polyoma and of most of the other oncogenic viruses, the relationships between spontaneous tumors and latent viruses and between host susceptibility and viral antibodies. Mammalian tumor viruses are classified into 2 groups: intranuclear and cytoplasmic viruses, the properties of which are compared. The author points out that the mechanism by which a virus induces cellular proliferation is unknown, even though specific viruses can generally be recovered from tumor tissue. Finally, the advantages of polyoma virus as a tool for studying experimental viral oncogenesis are stressed. (18 references)

- 63-164 DISTRIBUTION OF MAST CELLS AS A FUNCTION OF AGE AND EXPOSURE TO CARCINOGENIC AGENTS. (E.) Simpson, W. L. (Detroit Inst. Cancer Res., Mich.). Ann. N.Y. Acad. Sci. 103(Pt. 1):4-19, 1963.

After attempting to define a mast cell, the author reviews the recent literature on their distribution in the body and how this distribution is affected by age and exposure to carcinogenic agents. The number of mast cells varies greatly from tissue to tissue, and although there is some evidence that their concentration decreases with age, the chief determinants of the mast cell population would seem to be local factors. Increased numbers of mast cells in the contiguous connective tissue are quite commonly associated with epithelial hyperplasia and carcinogenesis, although the significance of this is unknown. See also CRA 1(2):#321, 1963. (34 references)

- 63-165 ANATOMY AND PATHOPHYSIOLOGY OF SKIN TUMOR CAPILLARIES. (E.) Urbach, F. (Temple U. Sch. Med., Phila.). Nat. Cancer Inst. Monogr. (10):539-559, 1963.

A broad review of the literature on the vascularization of benign and malignant tumors of the human skin, with particular emphasis on the author's previously published work with frozen sections prepared by the Gomori technic for alkaline phosphatase and with polarographic technics for the measurement of tumor tissue O₂ tension. In benign conditions, only minor changes are seen, but sections of malignant or even premalignant tumors show vigorous vascular proliferation with a marked increase in the number of dilated, elongated, tortuous

capillaries with many anastomoses and cross-anastomoses. Physiological studies, however, show a subnormal temperature in the tumor mass, puddling of dye in the tumor and generally low O_2 tensions. This is presumed to be due to the functional inefficiency of the tumor capillaries, resulting in slow, circular blood flow and tissue hypoxia, which may favor the development of those abnormal premalignant cells which are better able to survive on the basis of anaerobic glycolysis. (49 references)

63-166 THE ROLE OF THE STROMA IN EPIDERMAL CARCINOGENESIS. (E.) Orr, J. W. (Dept. Path. U. Birmingham Med. Sch., England). Nat. Cancer Inst. Monogr. (10):531-537, 1963.

In a review of the literature and his own published work, the author points out that systematic histological studies carried out during the long latent period required for chemical carcinogenesis reveals progressive changes in the dermis and subcutis but not in the continuously regenerating epidermal tissue. Besides, transplantation studies show that epidermis transplanted after treatment with a carcinogen does not develop a tumor at the new site, while tumors may develop at the treated site from epithelium which has never been in contact with carcinogen. It thus appears that the carcinogen has no direct effect on the epithelial cell but rather produces a permutation of the stroma, the complex changes in which lead eventually to neoplastic changes in the overlying epithelium. Experiments by A. T. Spencer are also reported showing that carcinomas and sarcomas could be induced in s.c. grafts of skin with much smaller doses of 20-methylcholanthrene (20 μ g) than are needed in situ. (26 references)

63-167 PENETRATION AND ABSORPTION OF IONIZING RADIATIONS IN SKIN. (E.) Tessmer, C. F. (Med. Gen. Lab. (406), US Army Med. Command Japan, San Francisco). Nat. Cancer Inst. Monogr. (10):393-406, 1963.

The author reviews the literature dealing with the characteristics of the energy transfer within the skin during irradiation with alpha particles, electrons, gamma rays, X-rays, neutrons, protons and heavier particles. He emphasizes that the tissue effects are identical for comparable amounts of all forms of radiation, but that the various components of the skin may differ in sensitivity. Generally, the basal-epidermal tissues, vascular endothelium and melanocytes are the most sensitive, with marked differences between species. Only X-rays and radium have so far produced carcinoma of the skin in man. In regard to the newer forms of radiation, probably insufficient time has elapsed to evaluate their latent periods. (73 references)

63-168 PRETUMOROUS CHANGES APPEARING IN OSSEOUS TISSUE UNDER EXPERIMENTAL

CONDITIONS UNDER THE INFLUENCE OF RADIOACTIVE ISOTOPES. (Rus.) Kraevskii, N. A. (Acad. Med. Sci. USSR, Moscow) and N. N. Litvinov. Vop. Onkol. 9(1):25-36, 1963.

In an extensive review of their own previously published work, as well as the work of a few others in the field of premalignant changes produced by radiation, the authors emphasize the importance of a thorough morphological study in order to contribute to the localization of the earliest changes and an evaluation of their reversibility. In discussing the necessary experimental technics and the use of model osteogenic tumors, they attempt to distinguish between changes in the background tissue, premalignant changes and the formation of an actual tumor. Some of the detailed changes observable in osseous tissue are described in chronological order on the basis of 5 yrs.' work with more than 3000 rats, dogs and rabbits given i.p. and i.v. injections of various concentrations (0.001-1.5 μ C/g) of a large variety of radioactive isotopes (Sr89, Sr90, Y91, Ce144, Zr95, Ca45, Ba140, various mixtures, or Pu239). The various diffuse and focal changes are related both to dose and site of action of the radiant energy, with emphasis on the effects of the optimal blastogenic dose (0.4 μ C/g) in young rats. Finally, the authors discuss the role of somatic mutations in the etiology of tumors, expressing doubt that the initial radiation injury produces any cells with the characteristics of neoplastic tissue. Rather, the eventual malignant transformation occurs only under the prolonged influence of the altered environment over the course of many cell generations. (18 references)

63-169 THE ROLE OF MELANOCYTES IN SKIN CARCINOGENESIS. (E.) Quevedo, W. C., Jr. (Biol. Dept., Brown U., Providence). Nat. Cancer Inst. Monogr. (10):561-575, 1963.

This review summarizes in one section current knowledge about the normal mammalian melanocyte, its distribution, reproduction, and participation in skin functions, especially in the cyclic growth of hair follicles. Another section, on primary melanocytic tumors, is concerned with spontaneous malignant melanoma in man, its histology and pathogenesis, and with experimentally induced melanocytic tumors of rodents (especially hamsters), their histopathogenesis and comparison with spontaneous rodent melanomas. In a section on melanocytes as secondary factors in tumorigenesis, the role of melanocytes in various tumors is outlined, with evidence for their correlations with malignancy, with growth activity, with coat color, with enzyme activity, and with genetic differences such as thickness of corneal layer. The interaction of melanocytes with epidermal cells, and their interdependence in normal and neoplastic physiology, are emphasized. (76 references)

63-170 VIRUSES AND SKIN TUMORS IN MAN AND ANIMALS. (E.) Coriell, L. L. (South

Jersey Med. Res. Found., Camden, N.J.). Nat. Cancer Inst. Monogr. (10):433-445, 1963.

The greater part of this review is devoted to a discussion of skin tumors which are caused or activated (in man and other animals) by viruses. The many and varied results of virus incorporation into cell-virus systems are enumerated, skin and mesenchymal virus-induced tumors listed, and some aspects of tumor immunity, together with possible mechanisms of tumor formation through viruses are considered. Some virus tumor diseases described include myxomatosis, molluscum contagiosum, warts, papillomatosis, fibromas, and polyoma virus tumors. Virus morphology, chemical composition and synthesis are briefly mentioned. (53 references)

63-171 SOME ASPECTS OF THE MORPHOLOGY OF EXPERIMENTAL PRECANCEROUS LESIONS. (E.)

Shabad, L. M. (Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). Pp. 111-118 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In a brief review of the characteristics of pre-carcinomatous and presarcomatous lesions in animals, based on the author's previously published work and that of his coworkers, he discusses the general patterns and stages of development of such lesions and attempts a more precise definition of precancerous processes, with particular attention to the etiological role of connective tissue changes and inflammation. The specific, often multicentric origin of each type of cancer is emphasized and 4 stages in the development of carcinoma are distinguished: a peculiar, diffuse, irregular, disproportionate hyperplasia is followed by the stage of focal growth and nodular proliferation, progressing into benign and then malignant tumors. Inflammation is not a precancerous process; precancer may be defined as a reversible, microscopic, multicentric, noninflammatory atypical growth of undifferentiated epithelium with a tendency to invasion but without destruction of the surrounding tissues. Finally, precancer is distinguished from such misleading concepts as latent cancer and carcinoma in situ. (28 references)

63-172 EXPERIMENTAL CANCER OF THE LUNGS. (E.)

Shabad, L. M. (Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). Fed. Proc. 22(2): (Pt.2):T331-T336, 1963. (Trans from: Arkh. Pat. 24(6):3, 1962.)

After reviewing some of the earlier attempts to produce experimental pulmonary tumors as a model for human lung cancer, including the induction of pulmonary adenomas in mice and the attempted production of pulmonary carcinomas in various species by the intratracheal, transthoracic or i.v. administration of coal tar or purified carcinogenic hydrocarbons (experiments which were mostly unsuccessful), the author mentions the positive results obtained with radioactive isotopes, by suturing the lungs with carcinogen-

impregnated threads or by occluding the bronchi with carcinogenic tablets. None of these technics led to the systematic production of large numbers of pulmonary carcinomas which would resemble human lung cancer. Described is some of the work which originated in his laboratory. Again, most of the early work (by Gritsiute) was negative, but the later work of Pylev, in which large amounts of 9,10-dimethyl-1,2-benzanthracene or 3,4-benzpyrene were introduced into the lungs of rats in combination with India ink by monthly intratracheal intubation, and development of lymphoid and connective tissue was impeded by simultaneous treatment with cortisone, led to diffuse hyperplasia, metaplasia and the eventual appearance of a considerable number of metastatic adeno- and squamous-cell carcinomas. The development of these tumors and some of the dose-response relationships are described. The success of these experiments is ascribed to proper selection of experimental animal, dose of carcinogen and method of application, and emphasizes the role of India ink in localizing the carcinogen for a sufficient length of time. (37 references)

63-173 EXPERIMENTAL ORAL CARCINOGENESIS. (E.)

Levy, B. M. (Dept. Path., U. Texas Dent. Branch, Houston). J. Dent. Res. 42(1) (Pt. 2): 321-327, 1963.

In this brief review on oral neoplasia, theoretical concepts and new developments in the field of carcinogenesis as they apply to the oral cavity are discussed. The various types of carcinogens, from radiation to viruses, are compared, and then the differences and similarities between the skin and the oral mucosa are pointed out, one of the major differences being that the skin is dry, with an outer layer of dead keratin, while the oral mucosa is wet and presumably alive. The oral mucosa has generally been found to be relatively resistant to carcinogenic agents. Finally, it is emphasized that the entire individual should always be taken into consideration in any discussion of local carcinogenesis, since the most appropriate interpretation of oral cancer is that it is a systemic disease which happens to have manifested itself in the oral cavity. (29 references)

63-174 THE ROLE OF SKIN NEOPLASIA IN TOBACCO CARCINOGENESIS. (E.)

Wynder, E. L. and D. Hoffmann. Pp. 61-71 in Tobacco and Health. James, G. and T. Rosenthal (Eds.). Springfield, Charles C. Thomas, 1962.

In a general review of the literature and their own published work, the authors outline the reasons for using mouse skin in the studies of tobacco carcinogenesis (similarity to bronchial epithelium combined with much greater ease of application) and emphasize that the purpose of such studies is not to prove the etiology of human lung cancer (arrived at by epidemiological technics), but to clarify the mechanisms of carcinogenesis and provide an assay system by means of which safer types of tobacco may be produced. The usual experimental

technic is described, after which some cigarette tar fractionation studies are reviewed in detail. These show that the carcinogenic components of cigarette tar are mostly isolated in the neutral fraction, particularly the CCl₄ eluate from a silica gel chromatogram of this fraction, in which there is a high concentration of 3,4-benzpyrene and other polynuclear hydrocarbons. In addition to these initiating agents, phenolic components are looked upon as cancer promoting agents. Finally, the possible preventive measures are reviewed, such as less inhaling, longer cuts, better filtration and, most important, elimination of at least some of the precursors of the carcinogens and promoting agents from the tobacco itself or from the smoke produced. (23 references)

63-175 THE SKIN AS AN ASSAY SYSTEM FOR POTENTIAL CARCINOGENS. (E.) Hueper, W. C. (NCI, Bethesda). Nat. Cancer Inst. Monogr. (10): 77-610, 1963.

In an extensive review of the literature, after dealing briefly with the scientific and practical significance of carcinogenic bioassays and the suitability of the skin as a bioassay system, various aspects of the problem are dealt with, such as the differences in technic between qualitative and quantitative testing. In reference to the latter, many factors are stressed: standardization of methods, the latent period, age, sex and strain of the animals, the solvent or vehicle, cocarcinogens and procarcinogens, viruses and chemical carcinogens, presensitization techniques and synergism, and, finally, carcinogenic antagonism and anticarcinogens. Also discussed is the care of the animals and test materials, the carcinogenic potency rating, and the biological criteria of cancerization of the skin, both in rapid tests using non-cancerous criteria and in long-term tests using criteria such as papillomas, histological findings, focal or diffuse cancerization, epidermal or dermal lesions, and s.c. sarcomas (which may or may not be significant). The author concludes that the skin is the most important, most useful and most commonly used bioassay system for the determination of the carcinogenic properties of physical and chemical agents, but that problems such as species and tissue specificity and the applicability of animal results to human preventive

medicine remain unsolved. The value of carcinogenic potency ratings would be greatly increased by the development of standardized testing procedures and uniform criteria. (244 references)

63-176 RESPONSIVENESS AND PROGRESSION OF THE MORPHOLOGICAL PRECURSORS OF BREAST CANCER IN INBRED MICE: A REVIEW. (E.)

Squartini, F. (Div. Cancer Res., U. Perugia, Italy) and G. Rossi. Pp. 319-327 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Mammary gland development from bud to advanced lobule, which is the first step in mammary carcinogenesis, was strictly hormone dependent. Less hormone-dependent, in high-cancer strain mice, were the hyperplastic alveolar nodules, progressing to greater autonomy with size, until frank mammary carcinoma became histologically recognizable. Some tumors at this last stage, may remain under hormonal influence. In RIII, a high tumor mouse strain, mammary tumors developed in 73.2% of breeding females and in 53.3% of virgins, at the average ages of 281 and 422 days, resp. These tumors were highly variable in their response to hormones, some growing during pregnancy and regressing after parturition, others regressing partially but resuming growth in following pregnancies, while still others grew steadily during and after pregnancy. Mammary tumor regression in response to ovariectomy was variable in the same or in different individual hosts. In RIII mice, progression toward hormonal unresponsiveness may not reach its end point within the life-span of the host. In C3H and in BALB/cf mice, most mammary tumors are of brief clinical duration, grow fast, rarely undergo partial regression, usually grow in a regular sigmoid curve, do not respond to pregnancy, originate from hyperplastic alveolar nodules, and are morphologically homogeneous. In RIII, most tumor growth is slow and prolonged, tumors often regress partially, grow irregularly, are responsive to pregnancy (hormones), originate in plaques, and are of varied cell composition. These inter-strain differences are of unknown origin, but the milk agent may be causally involved, since cross foster nursing resulted in RIII mice with tumors resembling and behaving like those of their BALB/cf nurses. Responsiveness and progression appear to be successive stages in carcinogenic development, with no sharp line of demarcation between them. See also CRA 1(1):#129, 1963. (23 references)

See also abstract nos.: 185,222,269

PHYSICAL CARCINOGENESIS

- 63-177 LESIONS CAUSED BY RADIATION. (Sp.) Ortiz Monasterio, F. (Gen. Hosp., Mexico, F. F.), A. Serrano Rebell, C. Sánchez Mota and M. Becerra. Gac. Med. Mex. 92(12):1023-1033, 1962.

In a study based on 139 pts. with lesions produced by radiations, the indications for radiotherapy, the high incidence of unnecessary exposure, the risks of faulty technic, and the frequency of incorrect diagnosis of radiation-induced lesions are discussed, along with the symptomatology and treatment (largely surgical) of radiodermatitis, and the risk of malignant damage. Post-radiation neoplasia, usually a late development, was diagnosed in 38 (28%) of the pts. in this series; 35 of the pts. had epidermoid carcinomas (4 with metastases), and 3 had sarcomas.

- 63-178 CARCINOMA OF THE SKIN. (Ger.) Winkler, K. (City Hosp., Berlin-Britz, Germany). Zschr. Aertzl. Fortbild. (Berlin) 51(10):773-785, 1962.

In a survey of primary skin cancers (basal cell and spinocellular carcinomas), the author discusses the diagnosis, prognosis, and treatment of their various forms and describes precancerous skin changes and pseudocarcinomatoses. While causes of malignant change are still unclear, factors believed to be of etiologic significance include sunlight and ionizing radiation, the former inducing basal cell carcinoma, the latter spinocellular carcinoma. The carcinogenic effect of X-rays and other ionizing radiations is greater than that of UV light. X-ray carcinomas developed after therapeutic irradiation led to solitary tumors while after insufficient protection in those exposed in their occupations, many foci developed. Latent period for X-ray cancer fluctuates between 7-34 yr. A single trauma rarely results in cancer development, but chronic mechanical irritation may lead to malignant change, as may suppurative and slow-healing wounds (e.g., balanitis, fistulas, and leg ulcers). Chemical agents which may lead to skin cancer include tar, paraffin, and lubricants. Long-term arsenic treatment is believed by some authors to lead to precancerous keratoses and ultimately to the development of basal cell and spinocellular carcinoma.

- 63-179 A LONG-TERM STUDY ON SUBJECTS WITH OCCUPATIONAL X-RAY AND RADIUM DERMATITIS (Czech.) Jirásek, L. (2nd Derm. Clin. Fac. Gen. Med., Charles U., Prague, CSSR) and M. Rejsková. Acta Univ. Carol. Med. (Praha) Suppl. 14:223-228, 1961.

Over an 8-year period, 137 pts. with occupational radiodermatitis have been observed, 112 of them medical workers, the other 25 in industry, research establishments, etc. Many have been

followed-up for over 5 yr. About one-half showed only degenerative lesions; in the other half there were moderately severe or severe proliferative changes. In mild cases, removal from the hazardous environment or the institution of protective measures led to partial recovery; in the moderately severe cases, the degenerative changes could be stabilized or retarded by environmental control. In the more severe cases, characterized by proliferative (precancerous) changes, the process could not be arrested and the danger of ultimate malignancy remained. Of 23 pts. with acute radiodermatitis, one later developed ulceration. Late ulceration with a tendency to malignant transformation was frequent in cases of chronic radiodermatitis. Carcinoma developed in 7 pts. several yr. after all exposure to ionizing radiation had ceased and in 5 pts. after rigorous protective measures had been in force for some yr.; in only 3 pts. did carcinoma develop earlier. Malignancy has now developed in 11% of the group of 137. There was no direct correlation between the severity of the skin lesions and changes in the blood picture.

- 63-180 THE PROBLEM OF POST-RADIATION LEUKEMIA. (Pol.) Blicharski, J. (3rd Clin. Int. Med., Cracow, Poland), J. Lisiewicz, L. Szczeciakowska and M. Wazewska-Czyzewska. Pol. Tygod. Lek. 18(11):384-387, 1963.

Three cases of leukemia in pts. exposed to massive doses of X-rays are reported. One, a 58-year-old woman, 2 yr. before diagnosis, had received 10 X-ray treatments of the spine (average dosage 1300 r) for painful ankylositic inflammation. The second pt., a 29-year-old man, admitted for hemorrhage after tooth extraction, had a WBC of 46,000 (82% myeloblasts). He had been exposed to X-rays some 60 times in a 3-year period, starting 8 yr. before onset of leukemia. The third pt., a 67-year-old man, developed lymphoid leukemia (WBC 145,000; 97% lymphocytes) 3 yr. after X-ray treatment of the temporal and cochlear region (11,000 r in 20 days) for plano-epithelial carcinoma. Lymph node biopsy revealed reticulosarcoma, and the post-mortem diagnosis was lympho-reticulosarcoma in the form of chronic leukemic lymphadenosis. The latency period in these cases is consonant with those reported in the literature for radiation-induced leukemia.

- 63-181 HISTOCHEMICAL AND CYTOLOGICAL STUDY OF EARLY BONE CHANGES DUE TO STRONTIUM⁹⁰. (Rus.) Kurshakova, N. N. (Acad. Med. Sci. USSR, Moscow) and A. S. Petrova. Blull. Eksper. Biol. Med. 54(8):104-107, 1962.

Studies of the metaphyses of the long bones in adult male white rats 15-280 days after administration of Sr⁹⁰ (0.4 mC/kg i.p.) revealed a progressive increase in alkaline phosphatase activity, the appearance of increasing numbers of atypical cells, and early signs of impaired osteogenesis,

long before any visible signs of osteosarcoma. Giant polymorphic cells with multiple nuclei and nucleoli, resembling tumor cells, first appeared among the large basophilic reticulocytes and osteoblasts at about the 125th day. The early increase in alkaline phosphatase activity may therefore be looked upon as a presarcomatous change.

63-182 ORAL EFFECTS OF INJECTED STRONTIUM 90. (E.) Rushton, M. A. (Guy's Hosp., London). *J. Dent. Res.* 42(1) (Pt. 2):340-342, 1963.

Examinations of the jaws of weanling rabbits 1 yr. to 9 mo. after a single i.v. injection of 100-1000 $\mu\text{C/kg}$ of Sr^{90}Cl revealed severe, dose-dependent changes in the teeth and surrounding tissues. Weanlings given at least 600 $\mu\text{C/kg}$, and which survived 6 mo. or more showed arrest of growth and eruption of the cheek teeth and consequent osteosarcoma. After 24 hr. pyknotic cells appeared among the differentiating odontoblasts. After 14 days, there was depletion of pulp cells, and at 30 days the growth of the cheek teeth had almost stopped. The incisors became progressively thinner, and most of the pulp was replaced by defective dentine. After 3 mo., vigorous proliferation of pleomorphic osteoblastic tissue appeared, succeeded within 6 mo. by multifocal osteosarcoma. Adult rabbits of less than 2 yr. of age, at the same dose level, showed similar but slower effects; those of more than 3 yr. of age showed less disturbance and considerable recovery of dental growth. In adults there were enormous accumulated doses in the mandibles and teeth, with severe bone damage, but delayed proliferative changes and incidence of osteosarcoma.

63-183 A CASE OF HEMANGIOSARCOMA OF THE LIVER 25 YEARS AFTER INJECTION OF THOROTRAST OR CEREBRAL ANGIOGRAPHY. (Dut.) Vellenga, L. (Rotterdam Harbor Hosp., The Netherlands). *Belg. Radiol.* 45(6):682-688, 1962.

Autopsy of the liver during a laparotomy for possible appendicitis in a 46-year-old Portuguese seaman revealed polymorphocellular hemangioendothelioma with an organized thrombosis and siderosis which was probably malignant, as well as an intracellular granular brown pigment which appeared to be thorium dioxide. Investigation revealed that the pt. had received 20 ml of Thorotrast in each carotid 25 yr. before (for the purpose of cerebral angiography), and that the liver tissue was radioactive. Following a detailed report of this case, the author reviews the literature on malignancy following Thorotrast.

63-184 PROPHYLACTIC USE OF CHLOROQUINE TO PREVENT SKIN CANCER. (E.) Knox, J. M. (Dept. Derm., Baylor U. Coll. Med., Houston) and G. Freeman. *Arch. Derm. (Chicago)* 87(3):315-322, 1963.

During a double-blind study of the effect of chloroquine on cutaneous carcinogenesis in pts. known to be susceptible to skin cancer, the incidence of new tumors (squamous-cell carcinomas and basal cell epitheliomas) in a placebo group and treated group were compared for periods of up to 35 mo. The inhibitory effect, especially as regards basal-cell epitheliomas, is believed to be due to neutralization of the carcinogenic effect of sunlight. In reference to earlier work, these results confirm the fact that exposure to sunlight is the most important factor in cutaneous carcinogenesis. Approximately 12% of individuals who have had 1 skin cancer will normally develop another within 6 mo., a figure which rises to 40% in a yr., 80% in 2 yr. and 90% in 2½ yr. Furthermore, among 100 pts. with skin cancer, 13 more malignant lesions will develop in 6 mo., 60 in a yr., 132 in 2 yr. and 197 in 2½ yr. More than 2/3 of these new cancers will be basal-cell in type. In the discussion, W. B. Guy suggested that basal cell epitheliomas, in contrast to squamous carcinoma, may not be the result of actinic exposure but rather a late manifestation of a seborrheic diathesis. This view, however, was refuted by others.

63-185 ULTRAVIOLET CARCINOGENESIS IN MAN. (E.) Daniels, F., Jr. (Dept. Derm., U. Illinois, Chicago). *Nat. Cancer Inst. Monogr.* (10):407-422, 1963.

In an extensive review, the effects of UV radiation on the different layers of the skin are discussed and these changes are examined in the context of possible loss of regulatory systems by the cells subjected to intense and prolonged exposure to sunlight. (37 references)

63-186 X-RAY INDUCED SKIN CANCER IN MAN. (E.) Traenkle, H. L. (Roswell Park Mem. Inst., Buffalo). *Nat. Cancer Inst. Monogr.* (10):423-433, 1963.

Reviewed are the types of X-ray-induced cancers, their induction, and hypothesis on the mechanisms of their genesis. X-ray-induced skin cancers in man may be squamous-cell, basal-cell, spindle-cell carcinomas, fibrosarcomas, rarely even malignant melanomas. While a definite threshold dose for carcinogenesis cannot be demonstrated, many small doses administered over a long period seem most likely to induce malignancy in X-ray dermatitis. Small, suberythematous doses, under 1000 r, and very large, skin-damaging therapeutic doses, induce no tumors. However, squamous cell carcinomas had resulted from large total doses (30,000 r) of very soft X-rays (grenz rays). Much of the evidence on carcinogenic X-ray dosage is conflicting. Variations in latency period are wide (3-48 yr.), and this has suggested an indirect extracellular carcinogenic mechanism. The variable incidence of malignant changes in pts. with radiodermatitis (less than 1% to 30%) is positively correlated with degree of tissue injury. Proposed mechanisms of radiation carcinogenesis range from speculations on the significance of alterations in the connective

tissue of the corium (collagen degeneration), epidermal damage, or vascular network alterations, to hypotheses of neoplasia based on the overdevelopment of a normal defense response to tissue injury, or on the change or inactivation of the enzyme systems regulating cellular respiration and/or the synthesis of new nucleoproteins. Additive and potentiating effects of cocarcinogens are also considered. (43 references)

- 63-187 AGE AT EXPOSURE AND THE LATE EFFECTS OF X-RAYS. SURVIVAL AND TUMOR INCIDENCE IN CAF₁ MICE IRRADIATED AT 1 TO 2 YEARS OF AGE. (E.) Kohn, H. I. (Radiol. Lab., U. Calif. Med. Ctr., San Francisco) and P. H. Guttman. Radiat. Res. 18(3):348-373, 1963.

Male and female CAF₁ hybrid mice were subjected to total-body X-irradiation (250 kvcp; 40-45 rads/min. for doses of 260 x 1, 260 x 2 or 520 x 1 rads) at the age of 385, 550 and 730 days (after 45%, 65% and 84% of the median life span). There was some increase in acute lethality with age at exposure, and irradiation had a general tendency to shorten survival time, but most of the differences were negligible; the life-shortening effect of irradiation was generally less in old adults than in young adults, and females were more sensitive to radiation than males until relatively late in life. The 585 tumors seen at autopsy included 323 pulmonary adenomas, 120 lymphocytic, myelocytic and reticulum cell tumors, 80 ovarian tumors and 62 miscellaneous (adrenal, gland, liver, Harderian gland, fibrosarcoma, hemangioma, etc.). The over-all incidence, was reduced by irradiation, and the survival time of the tumor-bearing mice was not affected; the fraction of animals with tumors was reduced from 68/82 to 123/172 in the male and from 69/81 to 182/235 in the female, but the number of tumors per tumorous animal was essentially unchanged. The authors conclude that the simple concept of premature aging is an unsatisfactory explanation of the effects of irradiation; some possible applications to human medicine are pointed out.

- 63-188 MALIGNANT INTRACRANIAL NEOPLASMS FOLLOWING RADIATION THERAPY FOR

ACROMEGALY. (E.) Goldberg, M. B. (Endocr. Clin., Dept. Med., U. Calif. Sch. Med., San Francisco), G. E. Sheline and N. Malamud. Radiology 80(3):465-470, 1963.

Four cases of malignant intracranial neoplasms (anaplastic epidermoid carcinoma, hemangioendothelioma, fibrosarcoma and an undifferentiated malignancy resembling a sarcoma), developing 10-30 yr. after irradiation, were detected among 75 pts. given radiation therapy for acromegaly. These 4 cases are reported in detail, and the 75 irradiated pts. are compared with 29 untreated acromegalic pts. with respect to sex, age at onset, duration of disease, time of irradiation (if any) and yr. of follow-up. Since the neoplasms all arose within or adjacent to tissues exposed to irradiation, since fibrosarcomas often develop in irradiated connective tissue, and since no sarcomas appeared in non-irradiated pts. with acromegaly, the authors conclude that the radiation therapy played an etiological role in these cases.

- 63-189 LEUKAEMIA AND IONIZING RADIATION IN JAPAN. AN EPIDEMIOLOGICAL SURVEY. (E.) Sakka, M. (Dept. Radiol., Tokyo Med. Dent. U.). J. Radiat. Res. 3(2):109-119, 1962.

Mortality rates from malignant disease in Japan have been increasing steadily; the rate for leukemia (per 100,000) was 1.3 in 1947 and 3.0 in 1958. In attempting to account for the increase, leukemia mortality rates in various parts of Japan were compared, where natural terrestrial radiation varied (17-118 mr/yr.), but no significant difference was found (314 cases among 12.8 million where terrestrial radiation was 27 mr/yr., and 446 cases among 20.3 million where it was 104 mr/yr.). Medical irradiation, calculated from the amount of X-ray film produced in Japan for radiography and photofluorography, has risen sharply between 1945 and 1960. However, the increase in leukemia mortality from 1950 to 1955 (1/100,000) was much greater than could be accounted for by the annual per capita accumulation of ionizing radiation from medical exposure. Leukemia deaths among radiographers (5 between 1951 and 1960), age-adjusted, did not show a significant proportional increase over those in the general population.

See also abstract nos.: 142,167,168,228,238,
241,273,281

CHEMICAL CARCINOGENESIS

63-190 TERATOGENIC EFFECT OF THE METHIONINE DERIVATIVES UPON THE MOUSE EMBRYOS. (E.) Nishimura, H. (Dept. Anat., Kyoto U. Fac. Med., Japan), M. Kageyama and K. Hayashi. Acta Sch. Med. Univ. Kyoto 38(2):193-197, 1962.

Methionine sulfoximine (0.05 mg/g/day i.p.) in pregnant Japanese dd mice, treated on days 9-15 of gestation, when sacrificed on day 18, resulted in 11/24 (46%) of mothers with malformed fetuses; among 195 implants, 45 (23%) were dead, 24 (16%) were variously malformed (5 clubfoot, 1 talipes calcaneovalgus, 2 digit maldirection, 8 eyelids open, 2 macrodactyly of the toe, 10 polydactyly of toe, and 3 tail anomalies). Among 30 other mice similarly injected with the glutamic acid antagonist methionine sulfoxide, in 3 dosages (0.1, 0.3 or 0.5 mg/g/day i.p., of 2, 6 or 10% solutions, resp.), 7/30 mothers produced malformed fetuses. Of 242 implants, 34 fetuses were dead; 9 fetuses were malformed (4 polydactyly of the toe, 1 maldirection of digit, and 5 clubfoot). Controls showed no malformations. Many embryos had been resorbed, or had died at various stages of development. The mechanism whereby the malformations are produced requires further study.

63-191 SMOKING AND LUNG NEOPLASMS. (E.) Noehren, T. H. (Buffalo). J.A.M.A. 183(5):398, 1963.

In reply to a question, the increase in bronchogenic carcinoma in women is real and significant. While in 1954, the death rate from respiratory cancer in white males was $4\frac{1}{2}$ times that of white females, later figures (1961, N. Y. State Bur. of Cancer Control) indicate that the relative increase in incidence of these tumors since 1942 has been 124.8% in women and only 70.2% in men. Squamous-cell carcinoma is the type commonly associated with cigarette smoking. Adenoma of the bronchus (which is essentially benign) and adenocarcinoma of the lung are not associated with cigarette smoking.

63-192 THE PHOTODYNAMIC EFFECT OF THE CARCINOGEN, 3,4-BENZOPYRENE, ON PARAMECIUM CAUDATUM. (E.) Epstein, S. S. (Child. Cancer Res. Found., Boston), M. Burroughs and M. Small. Cancer Res. 23(1): 35-44, 1963.

Cells from dark-grown, cloned cultures of Paramecium caudatum in suspensions of 3,4-benzopyrene (1×10^{-6} and 1×10^{-5} g/ml), upon irradiation with long wave UV, showed a 90% lethal effect after 1 min.; with 1×10^{-7} g/ml, after 4 min. and with 1×10^{-8} g/ml, after 18 min. This photodynamic response is a sensitized photooxidation, which is oxygen-dependent and could be inhibited by such antioxidants as

butylated hydroxy anisole and α -tocopherol, but not by others such as ascorbic acid. Other factors which modified the sensitivity of the photodynamic response were tryptophan, some plasma proteins, nonionic wetting agents, and inorganic salts. No evidence was found for the involvement of sulfhydryl groups or for peroxide formation in the photodynamic process. Other tested carcinogens were much less efficient, 90% lethal times of approximately 5-10 min. required a concentration of 1×10^{-6} g/ml of 1,2,5,6-debenzanthrane, and 1×10^{-5} for 9,10-dimethyl-1,2-benzanthracene and 20-methylcholanthrene.

63-193 THE DEVELOPMENT OF INDUCED TUMORS IN ANIMALS PREPARED BY PRELIMINARY SUBCUTANEOUS INJECTIONS OF BRAIN TISSUE. (E.) Timoshechkina, M. E. (Exp. Biother. Lab., Acad. Med. Sci. USSR, Moscow). Vop. Onkol. (Eng.) 7(11):63-67, 1961.

Groups of 125 C57 mice (3.5 mo. or older) and 135 rats were pretreated with a 10% homologous brain emulsion (0.3 and 0.5 ml, resp., s.c. x 3 at 5-day intervals); 15-18 days after the last injection the mice were treated with 9,10-dimethyl-1,2-benzanthracene by skin-painting with a 0.03% solution on alternate days for $3\frac{1}{2}$ mo. while rats received a single s.c. dose (in the flank) of 2 mg (in some cases this was repeated after 1-5 days). In mice, pretreatment significantly delayed tumor induction: the first papilloma appeared on day 59 in the treated group (day 31 in controls); the first cancerous tumor, on day 131 in the treated group (day 98 in controls). Squamous-cell cornified carcinomas developed in 63/70 controls, and 58/125 treated mice; incidence of papillomas was 66 and 90, resp. In rats, brain tissue pretreatment also delayed tumor induction of the first polymorphocellular sarcoma (154 days, controls 87 days) and led to fewer tumors (106/135, 78.5%; controls 74/80, 93%). Some tumors in the treated group were resorbed, which made histological verification difficult. After 470 days, mean tumor diameters in the treated and control groups were 14.2 and 33.2 mm, resp.; mean survival time in treated rats was increased by 228 days.

63-194 THE STUDY OF 3,4-BENZOPYRENE (CARCINOGENIC HYDROCARBON) IN THE HUMAN ENVIRONMENT. (Rus.) Shabad, L. M. (Oncol. Inst., Acad. Med. Sci. USSR, Moscow) and P. P. Dikun. Pp. 119-127 in Clinical Problems and Treatment of Malignant Neoplasms. V.7. Riga, Izdat. Akad. Nauk. SSSR, 1962.

In discussing the higher incidence of cancer of the lungs in highly industrialized areas, the authors consider the carcinogenic potential of the chemical substances to which man is exposed in such an environment, particularly in certain occupations. Studies of atmospheric pollution,

especially with 3,4-benzpyrene (BP), have been conducted in a number of cities in the USSR, using snow samples as well as sedimentation and aspiration methods. BP was found in all 250 snow samples from 18 towns, usually in significantly larger amounts in the larger cities, although the largest amount was detected in the smallest town studied. The amount also varied widely from one section to another of the same city. BP has also been detected in city soil samples, in oysters taken from the polluted water of ports, and in barnacles. The 4 main sources of atmospheric contamination by carcinogens are industrial wastes, smoke, exhaust fumes from vehicles, and dust from asphalt roads. Methods for controlling and preventing such pollution are assessed. Finally, the question of the possible carcinogenic effect of the continued exposure of human beings to small amounts of carcinogen is answered with a theoretical affirmative, on the basis of animal experimentation. The potential dangers of additive, cumulative effects, and sensitization are noted. BP has already been found in the lungs of human beings dying from causes other than cancer. In addition to the problem of the cumulative effect of small amounts of a single carcinogen, there is the further possibility of synergism between BP and other carcinogenic substances contaminating the atmosphere, such as 3,4,9,10-benzpyrene and certain aliphatic compounds, not to mention the contribution of tobacco smoke and ionizing radiation. That contributing factors other than atmospheric contaminants are required for the production of cancer is, however, obvious from the huge number of persons exposed to all of the noxious agents let loose in the large industrial city who do not develop the disease.

63-195 RECOVERY OF DEOXYRIBONUCLEIC ACID FROM THE EFFECTS OF ALKYLATION. (E.)

Strauss, B. S. (Dept. Microbiol., U. Chicago, Ill.). *J. Gen. Microbiol.* 30(1):89-103, 1963.

Treatment of a methionine-requiring strain of *Bacillus subtilis* with 0.025 M methylmethanesulfonate for 30 min. at 37°C induced a reversion frequency of 10⁻⁵ and decreased both the viable count and the transforming activity for an indole locus of DNA to about 10% of the original. Following alkylation either *in vivo* or *in vitro*, the transforming activity of DNA was sensitive to heating at 50°C, while normal DNA was resistant. However, the loss of transforming activity was not due to gross degradation since methylation and heating of DNA *in vitro* did not inhibit its uptake by competent organisms. When alkylated *B. subtilis* was incubated for up to 2 hr. in a medium supplemented with casein hydrolysate, methionine and tryptophan, the extractable transforming activity was more than doubled, while DNA in controls increased to 34%; the heat sensitivity of the transforming DNA from alkylated organisms also decreased during incubation. DNA synthesis was demonstrated in

the alkylated organisms by incorporation of thymidine-2-C¹⁴ without a lag period. These results indicate that alkylated DNA can serve as a template for the replication of DNA with normal activity.

63-196 THE EFFECT OF PROTEOLYTIC ENZYMES ON 3-METHYLCHOLANTHRENE-INDUCED SARCOMA.

(It.) Siliotti, I. (Obst.-Gyn. Clin., U. Padua, Italy), P. Grella and A. Bertolin. *Attualita Ostet. Ginec.* 8(5):601-614, 1962.

Trypsin + chymotrypsin (5 mg/day of each) were administered i.m. to 8/16 female Sprague-Dawley rats with 5-mo. s.c. tumors induced by 20-methylcholanthrene (10 mg s.c.; tumors developed in 16/26, 4/16 died of intercurrent disease). After 15 days, tumor volumes increased 215% in controls, 410% in enzyme-treated rats. Histologically and histochemically, the sarcomas in the treated and untreated groups were similar, but the administration of chymotrypsin + trypsin decreased tumor succinic dehydrogenase activity from about 170 to less than 20 µg of formazan/g tissue without affecting significantly the level in the liver or kidney. A 69-reference bibliography is appended, and published data on the results of proteolytic enzyme administration in human and animal cancers are summarized in a 4-page table.

63-197 COMPLEXES OF 3,4-BENZPYRENE AND VARIOUS SUBSTANCES IN AQUEOUS SOLUTION. SPECTROPHOTOMETRIC STUDIES. (It.) Prina, C. (Inst. Gen. Path., U. Pavia, Italy) and B. Magrassi. *Boll. Soc. Ital. Biol. Sper.* 38(23):1179-1182, 1962.

Solutions of 3,4-benzpyrene (BP) in chloroform were first examined with the UV Beckman spectrophotometer at all wavelengths from 2500-4000 Å, and the coefficient of extinction was determined so that concentrations of this substance in other, unknown solutions could be calculated. The ability of various substances to combined with BP was then ascertained, satisfactory (and reversible) combinations being achieved with caffeine, nicotinamide, and polyvinylpyrrolidone (PVP) (Subtosan). After chloroform extraction of BP from these compounds, its optical density curve was somewhat modified (disappearance of the peaks between 2500-3100 Å), which suggests that some modification of the BP molecule had occurred in these solutions, as it would seem to do in tissues. Whereas the affinity of caffeine and PVP for BP was maximal after 25-30 days, that of nicotinamide was greatest after 3 days. The proportion of BP in filtrates of the 3 solutions ranged from 10-12 µg/ml.

63-198 COMPOUNDS OF 3,4-BENZPYRENE AND VARIOUS SUBSTANCES IN AQUEOUS SOLUTION. *IN VITRO* AND *IN VIVO* ACTION ON EHRlich ASCITES CARCINOMA CELLS. (It.) Prina, C. (Inst. Gen. Path., U. Pavia, Italy), B. Magrassi and G. Roveta. *Boll. Soc. Ital. Biol. Sper.* 38(23):1183-1184, 1962.

Filtrates of 3,4-benzpyrene (BP; 10 mg, proportion not stated) made soluble in 40% nicotinamide (NC), 1% polyvinylpyrrolidone (PVP), 4% or 10% histamine dihydrochloride (H), and 1.5% caffeine (C) when added to Ehrlich ascites carcinoma cells *in vitro*, in all cases rendered fluorescent a number of cytoplasmic granules--probably lipids, since many stained with Sudan III. Injected into the peritoneum of normal mice and mice bearing 8-10-day-old ascites carcinoma, both BP + NC and BP + H caused rapid death, and cancer cells from treated tumor-bearing mice were devoid of fluorescent granules except in the immediate vicinity of the injection. The mixtures BP + C and BP + PVP were less toxic, but the staining of tumor cells observed *in vitro* was not seen in material from treated animals. Even when large quantities of BP, dissolved in oil, were injected i.p., it was difficult to demonstrate the staining reaction noted *in vitro*, indicating that other structures or substances in the living organism have a greater affinity for the hydrocarbon than the cytoplasmic granules. Moreover, when suspensions of tumor cells treated with the water-soluble BP mixtures were injected i.p. into normal mice, the granule fluorescence observed *in vitro* disappeared completely within 2 hr.; it also disappeared when such cell suspensions were injected s.c.

63-199 EARLY APPEARANCE OF AN ABNORMAL GLOBULIN IN THE SPLEEN OF DAB-FED RATS. (Fr.) Dufour, D. (Dept. Biochem., Fac. Med., U. Laval, Quebec, Canada). *Experientia* 19(1):42-43, 1963.

Hybrid (Fisher) rats were fed dimethylaminobenzene (DAB) for 2 mo. in a basic ration. After 6 wk. (and ingestion of 200 mg DAB), studies which utilized a rabbit anti-hepatoma immune serum revealed the presence of an antigen in spleen extracts from treated animals, but not in controls. Immunoelectrophoretic studies showed this antigen to be a globulin with slightly negative migration. At the time when this antigen appeared, the liver, kidney, thymus, serum, and lymph nodes did not contain the abnormal globulin and did not show any other qualitative change in antigen behavior. Thus, long before there was any sign of DAB-induced cancer of the liver, an abnormal globulin appeared--and probably originated--in the spleen.

63-200 SIGNIFICANCE OR NONSIGNIFICANCE OF PATHOLOGIC MITOSES IN THE ORIGIN OF EPIDERMAL TUMORS IN MICE. (Ger.) Setälä, K. (Path. Inst., U. Helsinki, Finland). *Verh. deut. Ges. Path.* 46:352-356, 1962.

A series of experiments is described in which pathologic mitoses induced by various techniques in high- and low-tumor mice were compared. In all, 62,500 mitotic figures were analyzed. Mitotic aberrations produced by 9,10-dimethyl-1,2-benzanthracene (DMBA), Tween 60, irradiation,

and mechanical irritation are illustrated and discussed. It was of particular interest that wounding alone produced the same type of pathologic mitoses in high-tumor CF-1 mice as were observed in malignant neoplasia. The healing process, normal in the low-tumor RA mice, was abnormal and delayed in the CF-1 mice. There was a statistically significant difference between the number of mitotic aberrations produced by agents other than DMBA in the 2 mouse strains; the high-tumor animals showed a far greater number ($P < 0.001$). However, the tumor-resistant mice also showed a significant number of aberrant mitoses after wounding of the skin, although no skin tumors developed. Thus the presence of pathologic mitoses in the mouse epidermis does not necessarily imply a malignant process, nor is it directly correlated with cellular proliferation. In fact, it is distinctly animal- or cell-dependent, and a sign of a hereditary latent potentiality (predisposition); that is, the mitotic response of certain cells shows a primary incapacity to react normally to noxious agents or trauma.

63-201 PRECANCEROUS CHANGES IN THE BREAST OF BALB/c/Cb/Se MICE INDUCED BY FOUR CHEMICAL CARCINOGENS. (E.) Biancifiori, C. (Inst. Morbid Anat., Div. Cancer Res., U. Perugia, Italy) and F. Caschera. Pp. 369-373 in *The Morphological Precursors of Cancer*. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Of 4 carcinogens (in almond oil, p.o.) administered to groups of 10 virgin and 10 pseudopregnant female BALB/c/Cb/Se mice, 9,10-dimethyl-1,2-benzanthracene (DMBA) induced, in pseudopregnant mice, the highest incidence of mammary tumors (60%) at the lowest dosage (9 mg) with the shortest latent period (14-30 wk.). 20-Methylcholanthrene (MC) at 12 mg; 3,4-benzpyrene (BP) at 15 mg; and 1,2:5,6-dibenzanthracene (DBA) at 15 mg, induced, resp., 38%, 35%, and 54% mammary tumors in 24-54 wk. Results in virgin mice were: DMBA, 5% in 18 wk.; MC, 6% in 42 wk.; BP, 0%; and DBA, 5% in 53 wk. Incidence of pathological lesions (nodules, adenomas; intraductal squamous metaplasia and papillomas; intraductal and intra-acinous carcinoma) in pseudopregnant mice was: DMBA 13/22; MC 3/14; BP 4/15; DBA 9/24. In virgin mice the only precancerous lesions were in the DMBA group (4/18). Precancerous lesions were more common (52%) among tumor-bearing than among non-tumor-bearing (12%) pseudopregnant mice.

63-202 OVARIAN TUMORIGENESIS WITH SPECIAL REFERENCE TO PSEUDOPREGNANCY. (E.) Mody, J. K. (Penrose Res. Lab., Zool. Soc. Phila.). Pp. 717-732 in *The Morphological Precursors of Cancer*. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

A large part of this review is devoted to the effect on the ovary, uterus and mammary gland of

IF mice of olfactory lobectomy and pseudopregnancy. When groups of 37 and 60 females were painted with 20-methylcholanthrene (20-Me) and 1,2,5,6-dibenzanthracene (DB), resp., there developed one early, doubtful ovarian tumor after 20-Me; DB led to no ovarian changes. After skin painting with 9,10-dimethyl-1,2-benzanthracene (DMBA) and 3,4-benzpyrene (BP) of groups of 60 and 53 females, there developed 12 and 4 induced ovarian tumors, resp.; all ovaries and follicles degenerated. In mice treated with DMBA and BP, the tumorous changes started with degeneration of all ova and follicles while the thecal cells aggregated and proliferated other luteinized cells (theca-lutein cells) in carcinogen-treated mice. Microscopic nodules then arose in the area of proliferated luteinized theca cells, the larger nodules became replaced by various tumors: granulosa cell type; mixed luteinized and granulosa cell mixed; thecal, luteinized and granulosa cell type; and luteoma. In the uterus, all but DB led to varying degrees of cystic glandular hyperplasia of the endometrium which only occasionally was associated with ovarian tumor. All agents led to the appearance of lobules in the mammary glands. In reference to the ovary, the author believes the histological evidence suggests that the altered thecal cell is the precise cell of origin of the granulosa cell series of tumors which develop.

63-203 GENERAL AND SPECIAL PROBLEMS IN THE ANALYSIS OF MALFORMATIONS, PARTICULARLY THOSE DUE TO THALIDOMIDE AND AMINOPTERIN DAMAGE. (Ger.) Werthemann, A. (Inst. Path., U. Basel, Switzerland). *Schweiz. Med. Wschr.* 93(5): 223-227, 1963.

After discussing the classification and terminology of prenatal pathology and dividing the entire period of human embryonic development into 4 stages (morpho- or blastogenesis, embryo- or organogenesis, fetogenesis and placental development), the author discusses some of the statistical difficulties in determining the incidence of congenital malformations. He points out that most malformations due to drugs or virus diseases occur during organogenesis, i.e. from the 3rd to the 8th wk. of gestation, while toxoplasmosis exerts its effects later, during fetogenesis. He then reports 2 cases of congenital malformations. In the first case, the mother was given thalidomide (15 drops/day x 5; total 0.375 g) in the 5th wk. of pregnancy to relieve headaches due to virus meningitis; the infant (born in the 8th mo. of pregnancy) showed complete lack of the left arm, phocomelia of the right arm, malformation of the legs, asymmetry of the kidneys, bilateral mega- and hydroureter, cryptorchidism, and slight anomaly of the outer ears. In the second case, the pt. took thalidomide (15 drops, 0.075 g/day) for insomnia during the first 5 wk. of pregnancy and aminopterin (0.5 mg x 6/day), in the 11th and 12th

wk., as an abortifacient. Miscarriage occurred in the 6th mo. While the mother only showed hair loss, the dead fetus was severely malformed, with hypoplasia of both thumbs, severe brachymetacarpus, bilateral brachydactyly, hypoplasia of the right leg with shortening of the fibula and compensatory curvature of the tibia, absence of some metatarsals and toes, syndactyly of some toes, faulty ossification of the cranium with severe malformations, and absence of lobulations in the lungs. The author concludes that thalidomide produces malformations by interfering with the metabolism of mesenchymal tissue during the critical stages of embryogenesis, while the aminopterin taken in the second case was probably responsible for the disturbance in cranial ossification and eventual death in utero.

63-204 ELECTRON DONATION AND ACCEPTANCE BY CARCINOGENIC COMPOUNDS. (E.) Allison, A. C. (Nat. Inst. Med. Res., London, N.W.7) and T. Nash. *Nature* 197:758-763, 1963.

After presenting data on the electron donor strength of a large number of carcinogens (hydrocarbons, steroids, aromatic amines and heterocyclic N compounds), both on the basis of the formation of charge-transfer complexes with chloranil in acetonitrile, with 1,3,5-trinitrobenzene in benzene and on the basis of electron spin resonance in complexes with tetracyanoethylene, the authors attempt to correlate this property with carcinogenicity. After pointing out some of the discrepancies, they show that there is also a broad correlation between carcinogenicity and electron acceptance, as in the reactivity with acridine. In order to explain the simultaneous ability to donate and accept electrons in a large number of carcinogenic compounds, the authors postulate a quinonoid or pseudo-quinonoid character due to lone pairs, and apply this theory to the different chemical classes of carcinogens; they also point out that steric factors and the stability of the carcinogen under physiological conditions play a role. Finally, this theory is related to biological systems by means of the "sandwich" model, in which the carcinogen lies between two active sites in a metabolic system, one an electron donor and the other an electron acceptor, forming charge-transfer complexes with both. On this basis, carcinogens may well exert a primary effect on oxidative phosphorylation. Tests demonstrating charge transfer with trinitrobenzene and acridine may also be useful as screening tests for possible carcinogens.

63-205 THE MORPHOLOGY OF EXPERIMENTAL BRAIN TUMORS. (Ger.) Schiefer, B. (Inst. Animal Path., U. Munich, Germany). *Acta Neuropath. (Berlin)* (Suppl. 1):19-25, 1962.

Implantation of pellets of 20-methylcholanthrene into the brains of mice and rats induced tumors in 40/151 animals which died after the 65th day

(the day of appearance of the first mesodermal tumor) including 13 neuroepithelial tumors (medulloblastoma, oligodendroglioma, glioblastoma; astrocytoma and ependymoma), 25 mesenchymal tumors (reticulum cell sarcoma, fibrosarcoma, polymorphocellular sarcoma, etc.) and 2 tumors of uncertain type (probably mesenchymal). The histological characteristics of each type are described in detail. The highly malignant nature of these tumors is pointed out and the problem of the development of polymorphocellular sarcoma within glioblastoma is discussed.

3-206 THE EFFECT OF CARCINOGENS ON MELANOCYTES. (E.) Szabó, G. (Mass. Gen. Hosp., Boston). Ann. N.Y. Acad. Sci. 100(Pt.1):269-78, 1963.

Biopsies of the dorsal skin or dorsal surface of the tail, taken at regular intervals from C57 black, CBA and C3H mice subjected to 1-2 applications of 0.15% 3,4-dimethylbenzanthracene (3,4-DMBA) in acetone followed by weekly applications of 0.5% croton oil in acetone for as long as 18 wk., revealed a marked increase in dopa-positive melanocytes in the normally pigmented areas of the caudal epidermis and their appearance in normally unpigmented areas, followed by aggregation of the melanocytes, inflammation and exfoliation; dopa-positive melanocytes also appeared in the normally negative dorsal epidermis, in the outer root sheath of the hair follicles and around sebaceous glands; in growing hair follicles, the normal dome-shaped structure of the matrix was disturbed so that pigmented epithelium bulged out toward the surrounding dermis, terminating in the formation of pigmented epidermal tumors in the dermis in close relationship to the hair follicles. These pigmented tumors were usually covered by apparently normal, unpigmented epidermis. These results indicate that the melanocytes of the hair matrix participate actively in the formation of pigmented tumors due to 3,4-DMBA.

3-207 N-HYDROXYLATION OF CARCINOGENIC AMINES IN VIVO AND IN VITRO WITH LIVER MICRO-SOMES. (E.) Uehleke, H. (Inst. Pharmacol., U. Tuebingen, Germany). Biochem. Pharmacol. 12(2):19-221, 1963.

The N-hydroxylation of 4-aminodiphenyl, aniline, 2-aminofluorene, 2-naphthylamine and 4-aminostilbene was confirmed both by the appearance of methemoglobin in the cat following i.p. injection of the carcinogenic amines (0.5 mM/kg), and by spectrographic estimation of the nitroso derivatives when the amines were incubated with rat liver microsomes and TPNH in phosphate buffer. In both cases, the rate of oxidation was highest for 4-aminodiphenyl and lowest for 4-aminostilbene. After injection of 4-aminodiphenyl, 4-aminodiphenyl could also be detected in the blood.

63-208 STUDIES ON HUMORAL FACTORS IN RAT SERUM AFFECTING THE PROTEIN METABOLISM OF EHRLICH ASCITES TUMOR CELLS. (E.) Koyama, S. (Dept. Surg., Niigata U. Sch. Med., Japan). Gann 54(1):19-25, 1963.

When glycine- C^{14} incorporation by Ehrlich ascites tumor cells *in vitro* was employed as a measure of protein metabolism, both normal rat serum and serum obtained shortly after partial hepatectomy had a marked stimulatory effect on uptake. This activity was destroyed by heating, but not by dialysis. One wk. after partial hepatectomy, however, the serum no longer stimulated glycine uptake, and it became inhibitory 14-20 days after hepatectomy. Similarly, serum from rats fed dimethylaminoazobenzene (DAB) was stimulatory (about equal to normal serum) for the first 30 days, and was able to counteract the inhibitory effect of serum obtained 14-20 days after hepatectomy. Serum from rats fed DAB for 4 days beginning 1 wk. after partial hepatectomy was particularly stimulatory, indicating an additive effect.

63-209 THE CARCINOGENICITIES OF FLUORO DERIVATIVES OF 10-METHYL-1,2-BENZANTHRACENE. II. SUBSTITUTION OF THE K REGION AND THE 3', 6-, AND 7-POSITIONS. (E.) Miller, J. A. (McArdle Mem. Lab., U. Wisc., Madison) and E. C. Miller. Cancer Res. 23(2) (Pt.1):229-239, 1963.

The carcinogenic properties of a number of fluorinated hydrocarbons were tested in adult female mice and adult male rats in 4 different ways: production of cutaneous carcinomas in mice by repeated application of the hydrocarbon to the skin (10-methyl-1,2-benzanthracene (MBA) 70 μ g or an equimolar amount of 1,2-benzanthracene (BA) in 0.025 ml acetone, x 2/wk. x 20); initiation of papilloma formation in mice by a single application of 300 μ g in 0.1 ml acetone, followed by 0.05 ml of 0.5% croton oil in acetone twice weekly for 23 or 38 wk.; induction of sarcomas by s.c. injection of 1.0 mg in 0.1 ml tricapylin in mice, or of 2.0 mg in 0.25 ml tricapylin in rats. In contrast to the 3'-fluoro-MBA, which is inactive, substitution of fluorine in the 4 position did not alter carcinogenic activity in rats and mice. The 3', 6- and 7- fluoro derivatives of MBA showed carcinogenic activity in 2 or more of the 4 tests, so that these positions do not appear to be directly involved in carcinogenic activity; the 6-fluoro derivative, however, was poor in the induction of s.c. sarcomas, while the 3'-fluoro derivative was poor in the induction of skin cancer. 4'-Fluoro-MBA was excessively toxic, but had considerable carcinogenic activity toward rat s.c. tissue. 1,2-Benzanthracene and its 3-fluoro derivative were essentially inactive in these tests. On the basis of these and previous data, the role of the K region in carcinogenesis by the polycyclic aromatic hydrocarbons is reviewed.

63-210 CONTRIBUTIONS TO THE PATHOGENESIS OF
EXPERIMENTAL VAGINAL CARCINOMA. (Ger.)

Lapis, K. (2nd Women's Clinic, Med. U. Budapest)
and B. Zsolnai. *Acta Chir. Acad. Sci. Hung.*
3(4):327-341, 1962.

20-Methylcholanthrene (20-Me; 1% in acetone) was applied intravaginally (tampon) in 130 adult rats every 2 days, later 2/wk., for up to approximately 1½ yr.; 15 rats also received croton oil, intravaginally, 1/wk. Some (15) received estrogen (5 U); 20 were castrated 6 wk. before treatment with 20-Me; 20 were castrated and given estrogen (5 U); 15 received testosterone propionate (20 µg); 15 received progesterone (5 U). Hormones were given s.c. 2x/wk. for 6 mo. Vaginal smears, culdoscopy examination and postmortem histological studies of the genitalia revealed very few changes during the first yr. (leukoplakia in 8 dead and 3 sacrificed among 22, at 7-9 mo. and 18/47 dead at 10-12 mo., atypical preblastomatous epithelial changes in 3/22 and 15/47, (but severe in only 1 and 2, resp.). Among 58 rats dead after 13-18 mo. (42 sacrificed), 12 still showed no histological changes in the vagina, 21 showed leukoplakia, 14 showed mild, 6 severe atypical epithelial changes, 1 developed carcinoma *in situ* (20-Me + progesterone), 1 developed a spindle cell sarcoma and 3 developed invasive carcinoma (1 from 20-Me + croton oil, 2 from 20-Me + castration and estrogen). There were no metastases in any case. The rat vaginal epithelium is thus quite resistant to the action of carcinogenic agents.

63-211 AUTORADIOGRAPHIC STUDIES ON DNA
SYNTHESIS DURING EXPERIMENTAL CAR-
CINOGENESIS OF THE LIVER PARENCHYMA OF THE RAT
BY MEANS OF DIETHYLNITROSAMINE. (Ger.) Côté, J.
(Inst. Path., U. Freiburg, Germany), W. Oehlert
and F. Büchner. *Beitr. Path. Anat.* 127(3):
450-473, 1962.

Autoradiographs of the liver parenchyma, prepared 30 min. after administration of tritiated thymidine (0.2 µC/g body wt., i.p.) to albino rats (150 g) given diethylnitrosamine (0.75 mg/day p.o.) for 15-130 days, showed increasing numbers of epithelial cells taking part in DNA synthesis, especially at the periphery but later also in the center of the lobe, as well as increasing vacuolization and cytoplasmic clearing, followed later by increasing numbers of mesenchymal cells taking part in DNA synthesis and eventually by the formation of isolated microcarcinomas (islands of proliferating, micronuclear cells with a strongly basophilic, homogeneous cytoplasm). These findings are compared with those in a rat with definite hepatic carcinoma. While necrotic cells were consistently found near those most actively engaged in DNA synthesis, a possible stimulatory effect on the replication of DNA seems improbable because of their low, relative frequency. The authors feel their results support the hypothesis of a controlling mechanism exerted

by cytoplasmic proteins on the nucleus and special on DNA synthesis.

63-212 PRIMARY REACTIONS OF CARCINOGENS WITH
CELLULAR SUBSTANCES, AND THEIR INHIBI-
TION. (Ger.) Schmid, H. (Inst. Phys. Chem.,
Tech. Coll., Vienna). *Naturwissenschaften* 50(2):
46-47, 1963.

On the basis of kinetic data published elsewhere, the author suggests that the primary reaction between a carcinogen and cellular substances is due to polarization of the carcinogen by the positively charged reactive sites on the polar molecules of the cell. Carcinostatic substances which are dipoles or positive ions therefore act by competing with the polar molecules of the cell for the carcinogen. If the cellular substances contain pyridine, purine or pyrimidine, then the carcinogen attacks the N atom in this heterocyclic ring; in other cases, it may attack the positively charged N atoms bound to iron in cytochrome C or the iron porphyrins. Carcinogens therefore interfere not only with the reduplication of DNA, but with a large number of enzyme systems in the cell, which explains why an excess of such cellular enzymes exerts a carcinostatic effect by competing with the DNA for the carcinogen.

63-213 THE CHARACTERISTICS OF CARCINOGENESIS
IN MUSCLES WITH VARYING TYPES OF
METABOLISM. (Rus.) Pozdnyakov, O. M. (Inst.
Norm. Path. Physiol. Acad. Med. Sci., USSR,
Moscow). *Biull. Eksper. Biol. Med.* 55(2):78-83,
1963.

When 9,10-dimethyl-1,2-benzanthracene (DMBA; 20 mg in 0.5 ml peach oil) was injected into either the thoracic (white) or femoral (red) muscles of 40 chickens (cocks), tumors developed (in 2-5 mo.) only in the thoracic musculature. Since the thoracic muscles differ not only in the content of myoglobin and other substances, and in the fact that they derive most of their energy from anaerobic glycolysis while the femoral muscles actively oxidize carbohydrates, but also in their function, innervation and vascularization, 30 additional chickens were given DMBA in either the thoracic or femoral muscles and were killed at intervals, beginning 3 days after injection, for purposes of histological study. This showed only quantitative differences, such as a more pronounced cellular reaction in the femoral muscles, up to the end of the first mo. after which qualitative differences appeared; the femoral muscles showed rapid resorption of the carcinogen. The first signs of malignancy appeared in the thoracic muscles at 51 days, and tumors eventually appeared in 9/20 chickens which survived 2 mo., including 8 with localized rhabdomyosarcoma and 1 with metastatic round cell sarcoma. The higher metabolic activity of the femoral musculature thus seems to contribute to an increased resistance to carcinogenic effects.

63-214 LEIOMYOSARCOMA OF THE EPIDIDYMISS DEVELOPING IN GOLDEN HAMSTERS FOLLOWING SIMULTANEOUS TREATMENT WITH TESTOSTERONE AND ESTROGEN. (Fr.) Rivière, M. R. (Lab. Exp. Med., Inst. Cancer Res., Villejuif, Seine, France), I. Chouroulinkov and M. Guérin. *C. R. Soc. Biol. (Paris)* 156(6):1033-1035, 1962.

Simultaneous treatment of 2-month-old male golden hamsters with testosterone propionate and diethylstilbestrol dipropionate (implantation of 100 mg and 25 mg, resp., repeated in 5 mo.) led to the formation of leiomyomas and leiomyosarcomas of the smooth muscle of the epididymis in all 17/20 hamsters which survived for more than 1 yr. (sacrificed at 12-13 mo.); pulmonary metastases were detected in 1 case, and there were also pathological changes in the pituitary, adrenals, thyroid, testes, liver and kidneys (epitheliomatous foci in 3 animals). Transplantation of 1 leiomyosarcoma was successful in 1/10 hamsters treated with testosterone and diethylstilbestrol and failed in 10/10 untreated controls.

63-215 CHANGES IN THE CUTANEOUS CONNECTIVE TISSUE OF THE RABBIT EAR DURING THE DEVELOPMENT OF TUMORS INDUCED BY 9,10-DIMETHYL-1,2-BENZANTHRACENE. (Rus.) Ou Pao-Hsiang (Inst. Exp. Clin. Oncol. Acad. Med. Sci., USSR, Moscow). *Biull. Eksper. Biol. Med.* 55(2):83-87, 1963.

Histological studies on the skin of the ear in rabbits following application of 9,10-dimethyl-1,2-benzanthracene (1% in benzene), either a single application or 3x/wk. for 38-279 days, showed that the processes of carcinogenesis (epithelial hyperplasia and cornification of the hair follicles leading to papilloma formation and eventually, in the 3rd mo., to malignant epithelial infiltration) were accompanied by marked changes in the connective tissue. Focal lymphocytic infiltration appeared early and persisted throughout the experiment, while proliferation of connective tissue fibroblasts was especially pronounced around the invasive epithelium. This proliferating connective tissue contained large amounts of chromotropic acid mucopolysaccharide. The basal membrane of the epithelium remained intact during the early stages of carcinogenesis, while during the stage of invasive growth newly developed basal membranes were observed around the epithelial nests. The author points out that the changes in the basal membrane during invasive growth of malignant tissue were essentially the same as those observed during benign inflammatory processes.

63-216 STUDY OF PHOCOMELIC MONSTERS IN CHICK EMBRYOS OBTAINED BY MEANS OF NITROGEN MUSTARD. (Fr.) Salzgeber, B. (Lab. Exp. Embryol., Coll. France, Paris). *C. R. Soc. Biol. (Paris)* 156(7):1219-1221, 1962.

Nitrogen mustard (0.01-0.00061 mg/egg, in aqueous solution) was injected into 192 White Leghorn chick embryos at embryonic Stages 17 to 21 (Hamburger and Hamilton); 26 died too soon for evaluation of limb development. Of the remaining, 53 died between days 7 and 10 and 113 were sacrificed between days 12 and 19. Malformations of skeletal cartilage were found in 151 (91%), the most characteristic being phocomelia, most common in embryos surviving after day 12. Less frequent skeletal abnormalities were neck torsion, microphthalmia, and, in embryos that died very early, a constriction of the trunk similar to that found following X-ray treatment. These chemical-teratogenic effects show the selective sensitivity of certain morphogenetic processes to specific chemical substances.

63-217 INDUCTION OF ESOPHAGEAL CARCINOMAS BY UNSYMMETRICAL NITROSAMINES. (Ger.) Druckrey, H. (Lab. Surg., U. Clin., Freiburg, Germany), R. Preussmann, G. Blum, S. Ivankovic and J. Afkham. *Naturwissenschaften* 50(3):100-101, 1963.

Nine different unsymmetrically substituted nitrosamines were administered daily p.o. to young BD rats for periods of up to 1½ yr. Ethyl-tert-butyl nitrosamine (80 mg/kg/day; LD₅₀ 1600 mg/kg, p.o.) produced no tumors, even after a total accumulated dose of 25 g/kg; ethylethanol-nitrosamine (20 mg/kg/day; LD₅₀ > 7,500 mg/kg, p.o.; latent period 260 days) produced only liver carcinomas. Also tested were the following compounds: (dose in mg/kg/day; latent period in days; LD₅₀ in mg/kg, p.o.): ethylvinyl- (1.3 - 240 - 88); ethylisopropyl- (10 - 392 - 1,100); ethyl-n-butyl- (5 - 237 - 380); and methylbenzyl nitrosamine (1 - 264 - 18); dimethyl-dinitroso-ethylenediamine (2 - 290 - 150), N-nitrososarcosine (200 - 430; - > 5,000); and N-nitrososarcosine-ethyl ester (50 - 185 - > 4,000). These compounds uniformly produced multiple squamous-cell carcinomas of the esophagus, with no involvement of the oral cavity or stomach. In the case of ethylisopropyl- and ethyl-n-butyl-nitrosamine, some liver tumors were also produced. The organospecific action of these compounds was confirmed by the appearance of esophageal carcinoma in another group of rats given N-nitroso-piperidine (10 mg/wk., i.v. during the latent period of 285-400 days). The negative results with ethyl-tert-butyl-nitrosamine confirmed the diazoalkane theory of nitrosamine carcinogenesis.

63-218 METHYLCHOLANTHRENE INDUCED BREAST CANCER IN THE RAT. STUDIES ON MECHANISM OF INHIBITION BY LARGE DOSES OF ESTROGEN. (E.) Shay, H. (Fels Res. Inst., Temple U. Sch. Med., Phila.), M. Gruenstein and W. B. Kessler. Pp. 305-318 in *The Morphological Precursors of Cancer*. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Of 70 female rats aged 2 mo., implanted with estradiol (E; 25 mg pellet, s.c.), 14 (20%) developed breast cancer within 12 mo.; mean latent period was 37.5 wk. Large pituitary tumors were induced (135.3 mg/100 g body wt.; controls 5.6 mg) and body wt. < (141.9 g; controls 244.8). Tace (chlorotrianisene; 1 mg/100 g body wt./day x 6/wk.) < body wt. but induced no tumors. MER-25, (5 mg/day x 6/wk.) produced no tumors but lowered mean body wt. somewhat (205.7 g) and pituitary wt. (3.84 mg). Ovine lactogenic hormone (LH, Panlitar; 2.5 mg/day x 6/wk. s.c.) for a year induced no tumors but stimulated mammary lobule-alveolar growth, increased body wt. (286.9 g), and decreased pituitary wt. (4.5 mg). Rats treated with 20-methylcholanthrene (20-Me; 2 mg) induced breast cancer in 81%; addition of E decreased tumor incidence to 38.1% but did not alter the latent period (27.6 wk. 20-Me alone; 29.8 wk. 20-Me + E). Tace and MER-25 plus 20-Me decreased tumor incidence to 51.3% and 33.3%, resp., and increased the latent period (38.1 and 35.9 wk., resp.). LH + 20-Me = 84% tumor incidence. Body wt. (g) and pituitary wt. (mg) were: 20-Me, 229.3 and 5.6; 20-Me + E, 145.3 and 117.4; 20-Me + Tace, 161.2 and 3.9; 20-Me + MER-25, 199.4 and 4.1; 20-Me + LH, 256.9 and 5.8, resp. Combination of 20-Me + E + Tace and 20-Me + E + MER-25 induced tumors in 66.7% and 35.7%, resp.; body wt. were 138.9 and 145.4; pituitary wt. 53.9 and 70.8. 20-Me + E + LH, induced 43.4% tumors; body wt. was 152.5; pituitary wt. 110.7. Tace and MER-25 partially reversed the effect of E on pituitary wt. but did not alter its effect on body wt. All rats receiving large doses of E developed large pituitary adenomas and their body wt. decreased. Wherever this effect of E on the pituitary occurred in female rats receiving 20-Me, the induced breast cancer was significantly reduced. This inhibition results from suppression of a pituitary factor(s) by the estrogen. This cocarcinogenic pituitary factor is not a lactogenic hormone, gonadotropin, or growth hormone.

- 63-219 SALICYLATE-INDUCED MALFORMATION IN MOUSE EMBRYOS. (E.) Larsson, K. S. (Wenner-Gren Inst., Stockholm), H. Boström and B. Ericson. *Acta Paediat. (Stockholm)* 52(1): 36-40, 1963.

Sodium salicylate (10 mg x 1, i.m.) given on day 12 or 13 of pregnancy, in six A/Jax mice led to the production of four 18-day embryos with spots of discolored tissue (encapsulated blood) on the nose and/or chin or paws, and one with grossly abnormal paws; one resorbed all 10 embryos. Among these, and among 18 other mothers similarly injected on gestation day 7-11, there was a high incidence, among the offspring, of deformities of the ribs and vertebrae. These disturbances of vascular and skeletal development may be due to the inhibition of mucopolysaccharide formation by salicylates. A possible role of salicylates in human teratogenesis too is suggested.

- 63-220 RESEARCH ON THE IN VIVO CARCINOGENIC ACTIVITY OF AN IRON-DEXTRAN COMPLEX IN THE RAT. (Fr.) Viallier, J. (Lab. Exp. Path., Pasteur Inst. Lyon, France) and M. Rebouillat. *C. R. Soc. Biol. (Paris)* 156(4):691-693, 1962.

Administration of an iron-dextran complex containing 50 mg/ml of Fe to adult Wistar rats (0.1 ml/wk i.m. for periods up to 15 mo.) led to the appearance of only 1 case of bladder sarcoma (after 22 injections in 14 mo.) and 2 cases of mammary carcinoma (14 injections in 6 or 7 mo.) among 30 animals. In a second experiment with 98 rats, weekly injections of 0.2 ml of iron-dextran for up to 51 wk. led to only 1 case of lymphosarcoma. No tumors developed at the site of injection.

- 63-221 ELECTRON MICROSCOPY OF THE EXPERIMENTAL AZOIC HEPATOMA OF THE RAT. II. "ULTRA-FINE" CHANGES IN THE CYTOPLASM. (Fr.) Driessens, J. (Lab. Exp. Med., Inst. Cancer Res., Lille, France), A. Dupont and A. Demaille. *C. R. Soc. Biol. (Paris)* 156(10):1648-1649, 1962.

Electron microscopy of 10 rat malignant hepatomas induced by injections of 3'-methyl diethylaminoazobenzene (reported as 3' methyl diethylamino-benzene, 3' Me DAB) in combination with a deficient diet revealed changes in the ultrastructures of the nucleus and nucleolus, the endoplasmic reticulum, the mitochondria, the ergastoplasmic-mitochondrial complex and certain cytoplasmic inclusions, all of which are briefly described. Some of the more significant findings were lipid inclusions in the nuclei resembling those previously reported in transplantable mouse hepatoma or toxicity due to colchicine or thioacetamide, marked degeneration of the mitochondria, dilatation of the ergastoplasmic sacs, and the appearance of unidentified osmiophilic droplets or granular plaques in the cytoplasm.

- 63-222 MECHANISM OF SKIN TUMORIGENESIS IN MOUSE (E.) Niskanen, E. E. (Dept. Path., U. Helsinki, Finland). *Acta Path. Microbiol. Scand. (Suppl. 159):*5-77, 1962.

Histological studies of the dorsal skin of 2-3-month-old virgin female mice of the tumor-resistant RA strain, up to 30 days after a single gastric instillation of either urethan (U; 1-16 mg), 20-methylcholanthrene (MC; 0.1-1.6 mg) or 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.1-1.6 mg) revealed irregular epidermal hyperplasia, particularly in the perifollicular regions, with elongated and compactly-built basal-type cells arranged in several layers, cell surface stickiness, unevenly layered differentiating cells of variable size, disturbances in keratinization, sometimes destruction of hair as well as atrophy of the sebaceous glands, a slight increase in mitotic activity and, quantitatively, an increase in the total number of cells with a decrease in the percentage of basal cells and an increase in

the percentage of differentiating cells. These changes were unrelated to dosage. In contrast, application of Tween 40 to the dorsal skin, 6/wk. for 30 days, produced only a regularly-built hyperplasia in the interfollicular epidermis (IFE), and the pilosebaceous apparatus was preserved. When the applications of Tween 40 were begun 30 days after a single gastric instillation of carcinogen, some of the changes noted for the carcinogen alone were accentuated, both qualitatively and quantitatively. Now, however, the areas of irregular IFE hyperplasia and derangement of the pilosebaceous apparatus alternated, particularly in the case of U, with areas where regularly-built hyperplasia prevailed. There were generally more basal cells and fewer differentiating cells than after Tween 40 alone. Again, the cutaneous changes were generally unrelated to the dosage of carcinogen, except possibly in the case of DMBA, and were unaffected by the phase of the hair follicular cycle. In subsequent experiments, application of Tween 40 was continued for 38 wk. Following U (16 mg) + Tween 40, maximal incidence of focal skin tumors after 38 wk. was 13%; a dose of 1 mg produced no tumors, but at intermediate dosages there was little correlation with rate of tumor development. Following MC (0.2-1.6 mg) + Tween 40, maximal tumor incidence of 14-17% occurred after 34-38 wk.; a dose of 0.1 mg produced a tumor incidence of only 7.5%, but otherwise there was little correlation between dose and rate of tumor development. Following DMBA (1.6 mg) + Tween 40, after 32-38 wk. maximum tumor incidence was 53%; incidence after 0.1 mg was 18%. With DMBA there was a definite correlation between dosage and rate of tumor development. All the skin tumors were benign keratinizing papillomas and keratoacanthomas, and many of them regressed spontaneously; there were no skin tumors outside the area of application of Tween 40. Autopsy, however, revealed, in mice given U, 3 bronchial adenomas; in a mouse given MC, bronchial adenomas also. In mice given high doses of DMBA, there were a variety of malignant tumors (metastatic ovarian carcinoma, leukemoid reaction, anaplastic bronchial carcinoma, granulosa-cell tumor of the ovary, and retroperitoneal sarcoma with pulmonary metastases), which significantly shortened survival time. Control studies with either Tween 40 alone or Tween 40 after a single dose of Carbowax 100 led only to 1 skin tumor in each case. On the basis of the results of this study and a review of the literature (54 references), the differences between the effects of carcinogens and of tumor promoters are pointed out.

63-223 INDUCTION OF NEOPLASMS IN PLANARIANS WITH CARCINOGENS. (E.) Foster, J. A. (Stanford U. Sch. Med., Calif.). Cancer Res. 23(2):300-303, 1963.

Treatment of planaria (*Dugesia dorotocephala*) with 1,2-benzanthracene (BT), 3'-methyl-4-dimethylaminoazobenzene or 3,4-benzpyrene (4 ml of saturated alcoholic solution added to medium for 24 hr./wk. over a period of 3 mo.) resulted in nodular growths in 9%, 6% and 5% of the animals,

resp., the first tumor appeared after 1 mo. Treatment with BT for 2 mo. followed by transverse section resulted in nodular growths in 21% of the regenerating sections after 10-20 days. The lesions appeared on the pigmented back of the planaria, increased in size, became necrotic and eventually caused death in 10 days to 1 mo. Histologically, the lesions resembled mammalian tumors, with highly basophilic nests of macronuclear cells invading the intestinal tract, excessive pigmentation, giant cells and cells containing pigment globules in the subepidermal layer underlying areas of epidermal hyperplasia, and invasive intestinal hyperplasia with numerous mitotic figures and pyknotic nuclei. The classification of these neoplasms, however, remains unclear.

63-224 BIOCHEMICAL CHANGES IN GUINEA-PIG CORNEA FOLLOWING CARRAGEENAN INJECTION. (E.) Praus, R. (Czech. Acad. Sci., Prague) and J. Obenberger. Exp. Eye Res. 2(1):53-64, 1963.

Biochemical studies carried out on the corneas of adult guinea pigs 3-32 days after injection of carrageenan (0.02-0.04 ml, 1% in saline) into the central part of the corneal stroma showed > in fresh and dry wt. and water content, with a maximum on day 10, a parallel > in hexosamine (but < in concentration), a gradual < in hydroxyproline content, and a rapid > in incorporation of ³⁵S with an initial maximum on day 6 and a second on day 20. Macroscopically, the cornea became cloudy, thickened and convex, and newly formed vessels appeared with occasional small hemorrhages; the cornea swelled considerably, and granuloma formation was complete by about day 10, followed by thinning of the cornea and a gradual return to a normal appearance, with clearing from the periphery towards the center between days 25-32. The results are interpreted as indicating tissue swelling, mucopolysaccharide accumulation and possible glycoprotein accumulation, but no synthesis of collagen.

63-225 THALIDOMIDE AND CONGENITAL ABNORMALITIES. (E.) Yang Tsu-Ju (Inst. Zool., Acad. Sinica, Nankang, Taipei, Taiwan), Yang Tzu-Szu and Liang Hsu-Mu. Lancet 1:552-553, 1963.

Thalidomide injection (2.5 mg) into egg yolk sacs of chick embryos within 48 hr. of incubation produced amelia of the leg, oligodactylia of the 2nd and 3rd toes, and hemimelia of the wing. Injection after 72 hr. of incubation produced no limb deformities. Beak malformations (5/84) and acrania were found when thalidomide was injected as late as 9 days after incubation.

63-226 PATHOLOGICAL ALTERATIONS IN THE INCIPIENT STAGE OF LIVER CARCINOMA. (E.) Heinlein, H. (Inst. Path., U. Cologne, Germany). Pp. 191-188 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Dimethylaminoazobenzene (DAB; 30 or 20 mg/day, total of 600-1900 mg) added to the diet of male Wistar and hooded E-3 rats 10 days after

administration was stopped, produced: symptoms of cell irritation, benign adenoma, and hepato-cellular carcinoma. Incorporation rates of amino acids 90 min. after i.p. tritiated dl-leucine, l-phenylalanine, or dl-lysine showed that activity in adenoma cells was increased 1.9 times, and carcinoma by 2.5 times, over that of cells which showed only irritation. Incorporation of amino acid into nuclear protein was proportional to nuclear volume. Cytoplasmic incorporations, in the change from normal to malignant cells (cytoplasmic/nuclear activity ratios) were: normal livers, 8.2; irritation stage, 6.6; adenoma, 2.4; carcinoma, 0.94. With this progressive decrease in the cytoplasmically synthesized cell protein, concomitantly the nucleocytoplasmic ratio changes, from 1:7.39 in irritated cells, to 1:3.69 in adenoma, to 1:0.84 in carcinoma. Histochemically, cholinesterase and lipids were decreased in adenoma cells; carcinomatous liver tissue showed little enzyme activity. The mitochondria in carcinoma cells appeared to be profoundly altered so that the activity of the specific dehydrogenases were no longer detectable.

- 63-227 INTRAHEPATIC TOPOGRAPHICAL DISTRIBUTION OF PROTEIN-BOUND DYE AS REVEALED BY ^{14}C -LABELED 4-DIMETHYL-AMINOAZOBENZENE AUTORADIOGRAPHY. II. STUDIES ON RAT LIVER MODIFIED BY PROLONGED FEEDING OF BUTTER YELLOW. (E.) Baba, T. (Div. Path. Nat. Cancer Ctr. Res. Inst., Tokyo) and S. Takayama. Gann 54(1):105-108, 1963.

A male Wistar rat (140 g), prepared by feeding of dimethylaminoazobenzene (DAB; 837 mg over 168 days), after a 3 wk. rest period, was given DAB- ^{14}C (15 mg in oil/day \times 2, p.o.) followed by a diet containing 0.06% DAB for 50 hr. until time of sacrifice. Autoradiographic studies of the liver revealed the largest amount of radioactivity in areas of benign nodular hyperplasia with less in foci of atypical hyperplasia which could be considered premalignant. There was also some radioactivity in the Kupffer cells, but practically none in the biliary duct system. The results show that the proteins responsible for the binding of azo dyes are lost from the liver cell during the transition to malignancy.

- 63-228 EPITHELIAL TISSUE OF THE SKIN DURING CARCINOGENESIS. (E.) Glucksmann, A. (Strangeways Res. Lab., Cambridge, England). Nat. Cancer Inst. Monogr. (10):509-529, 1963.

Comparative studies on rats and mice subjected either to topical application of chemical carcinogens (1% solutions of 3,4-benzpyrene and 9,10-dimethyl-1,2-benzanthracene (DMBA) in acetone, 1/wk. to the dorsal skin or vulva) or to irradiation (0.7-1.0 mev electron beam or 200 kv X-ray) showed that chemical carcinogens have a direct effect on the epithelium and induce cancers in the descendants of treated cells, while irradiation is followed by malignant changes in the immigrating cells engaged in repair and hence

exposed to the progressive vascular damage induced by irradiation in the stroma. Chemical treatment induced in the dorsum of rats 15% papillomas, 84% carcinomas, 37% sarcomas (in mice results were 38% 48% and 0%, resp.). Comparable results in the vulva were equal for the 2 species (rats-22%, 62% and 2%; mice - 23%, 57% and 0%). Mouse dorsum reacted like the vulva, rather than rat dorsum; latent period in the mouse was also shorter. Some of the differences between rat and mouse skin, both normally and during the complex dermal and epidermal changes accompanying chemically-induced hyperplasia, are reviewed in detail, and it is pointed out that the steps leading to epidermal anaplasia are not correlated with characteristic stromal changes. In rats, irradiation led to 8% carcinomas and 32% sarcomas, compared to 20% and 40%, resp., for irradiation + DMBA; the induction period was also much longer after irradiation than after chemical treatment. Prior radiation increased the induction period for chemically-induced carcinomas, although slightly reducing it for sarcomas (compared to DMBA induction). Differences in response at various sites on the same animal are also discussed, as well as the effect of castration, pelvic irradiation, or administration of thiouracil or thyroxine to castrated rats. It thus appears that complex subtle forces play a role in affecting the response of different tissues to carcinogenic stimuli.

- 63-229 STUDIES ON PROMOTING ACTION IN SKIN CARCINOGENESIS. (E.) Saffiotti, U. (Inst. Med. Res., Chicago Med. Sch.) and P. Shubik. Nat. Cancer Inst. Monogr. (10):489-507, 1963.

A number of substances were tested for carcinogenic promoting activity in Swiss mice by applying them twice weekly to the clipped dorsal skin, beginning 1 wk. after a single application of 9,10-dimethyl-1,2-benzanthracene (DMBA; 1-1.5% in mineral oil). Tests with silver nitrate (10% aqueous), iodoacetic acid (0.9% in acetone), fumaric acid (1% in acetone), ethylphenylpropionate (5% in acetone), trihydroxymethylanthraquinone (Emodin; 0.5% in acetone), oleic alcohol, monostearin (5% in acetone) and sorbitan monolaurate were essentially negative although some of the agents produced marked epidermal hyperplasia; when a single application of croton oil (5% in mineral oil) was interspersed between the carcinogen and silver nitrate, 6/20 mice developed 14 benign tumors and 1 carcinoma. n-Dodecane showed moderate promoting activity (26 tumors, with 2 carcinomas, in 12/30 mice). Tests of several petroleum fractions showed high initial promoting activity (404 tumors, with 31 carcinomas in 36/50 mice), but the activity disappeared on storage, while there was no carcinogenic activity in mice, in New Zealand albino rabbits the petroleum fractions alone produced considerable numbers of tumors. One application of DMBA, however, did increase tumor incidence and shorten the latent period. The hexane-eluted fraction of a methanolic extract of croton seeds (which had little vesicant activity), had all the promoting activity of the original croton oil; this could be demonstrated

with urethan (20 mg/day i.p. for 5 days) as the initiator as well as with DMBA. In conclusion, the authors distinguish sharply between the promoting activity of compounds such as croton oil, which lead mostly to benign tumors (many of which regress spontaneously), and the additive effects of carcinogenic substances which may have a stimulatory effect on the second stage of carcinogenesis; for this additive carcinogenic effect, they suggest the term "developing action". Other studies on croton oil are also reviewed (66 references).

63-230 A MORPHOLOGICAL STUDY OF MAST CELL REACTION IN CHEMICAL SKIN CARCINOGENESIS OF MOUSE. (E.) Rizzi, I. (Inst. Morbid Anat., Div. Exp. Cancer., U. Bari, Italy) and L. Fiore-Donati. Pp. 515-527 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

A single application of 250 µg of 9,10-dimethyl-1,2-benzanthracene in acetone to the dorsal skin of female Swiss mice during the resting phase of the 2nd hair cycle produced ulceration followed by regenerative hyperplasia of the epidermis and hair follicles in most cases, and led to papillomas (true papillomas and keratoacanthomas) after an average latent period of 39 days in 73/130 animals which were allowed to survive. Progressive accumulation of mast cells, became evident 15-30 days after painting, throughout the superficial layers of the dermis; this mast cell response is roughly proportional to the degree of both epidermal hyperplasia and dermal fibrosis. The accumulating mast cells differed from normal mast cells, being smaller, hypogranulated and slightly metachromatic and exhibiting a characteristic primary golden-yellow fluorescence in UV light (which apparently is caused by an abnormally high content of 5-hydroxytryptamine). The mast cells lying in the deepest part of the dermis and in the subcutaneous tissue, in contrast, showed no changes in number and morphology during cutaneous carcinogenesis.

63-231 TUMOUR PROMOTION BY LIME OIL IN THE FORESTOMACH OF THE MOUSE, WITH A NOTE ON EARLY HISTOLOGICAL EFFECTS OF LIME OIL AND OTHER SUBSTANCES. (E.) Salaman, M. H. (Dept. Cancer Res., London Hosp. Med. Coll., England) and W. E. H. Peirce. Pp. 55-60 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Single doses of 9,10-dimethyl-1,2-benzanthracene (DMBA; 100 µg) or 3,4-benzpyrene (BP; 12.5-200 µg), dissolved in polyethylene glycol (PG) 400, were administered to mice by stomach tube, followed in 3 wk., in some mice, by treatment with undiluted lime oil (LO; 0.05 ml/wk. x 40, by stomach tube). Combined treatment with DMBA resulted in an average of 5.8 tumors in 13/13; without lime oil, there were an average of 2.6 tumors in 12/15 mice. After combined treatment

with BP (200 µg, 50 µg, 12.5 µg) there was an average of 3.4, 2.0 and 1.0 tumors in 15/17, 9/11 and 10/16 mice, resp; without lime oil average no. of tumors was 1.1, 0, and 0.2 in 5/13, 0/13 and 2/13 mice, resp. LO alone produced tumors in 4/24 mice (total of 6 papillomata). Most tumors were benign, but 2 cases of squamous-cell carcinoma appeared in mice given the highest doses of the 2 carcinogens + LO. In further studies, mouse stomachs were examined histologically 2-10 days after 1-2 doses of various agents. Croton oil, PG and phenanthrene had no effect on the gastric mucosa, while DMBA produced inconsistent, slight, uniform hyperplasia. In some mice, BP produced gross hyperplasia, with downgrowths of imperfectly differentiated squamous epithelium into the sub-epithelial tissue, while in other mice the hyperplasia was very slight. After administration of LO, there were large areas covered with abundant inflammatory exudate, under which there was necrosis, ulceration and infiltration of the sub-epithelial layers by inflammatory cells; there was also gross hyperplasia of the squamous epithelium, but the downgrowing hyperplastic epithelium was well differentiated and regular.

63-232 DINITROPHENOL INHIBITION OF PITUITARY ADENOMA FORMATION IN MICE FED PROPYL-THIOURACIL. (E.) King, D. W. (Roswell Park Mem. Inst., Springville, N.Y.), F. G. Bock and G. E. Moore. Proc. Soc. Exp. Biol. Med. 112(2):365-366, 1963.

Administration of 6-propyl-2-thiouracil (PTU; 10-12 g/kg diet) to C57Bl mice for periods up to 17 mo. produced benign pituitary adenomas weighing an average of 10-18 mg in 62%-72% of surviving mice. When dinitrophenol (DNP; 0.5 g/kg) + PTU was added to the diet, pituitary adenomas weighing an average of only 5-9 mg appeared in only 10%-15% of surviving mice. No tumors were observed in control mice fed DNP alone; the thyroid histologically was normal.

63-233 EXPERIMENTAL PULMONARY ADENOMA DUE TO URETHAN IN THE MOUSE. I. HISTOLOGICAL STUDY. (Fr.) Driessens, J. (Lab. Exp. Med., Inst. Cancer Res., Lille, France), A. Clay, J. Vanlerenberghe and L. Adenis. C. R. Soc. Biol. (Paris) 156(4):655-657, 1962.

Histological studies of the lungs in 50 Swiss mice given ethyl urethan (5 mg/day in the drinking water) for periods of 1-20 wk. revealed no macroscopically visible changes until about the 15th wk., progressing by the 20th wk. to well-delimited spherical adenomas. Microscopically, there was simple hyperplasia for the first 8 wk., followed by nodule formation progressing to typical papillary adenoma; in some cases in which urethan treatment was stopped, the tumorigenic process nevertheless continued. After the 20th wk., malignant transformation of the adenomas was sometimes observed. Pulmonary adenomas apparently originate in the alveolar wall and not in the bronchi.

- 63-234 SARCOMAS AT THE SUBCUTANEOUS INJECTION SITES OF TRYPAN BLUE IN THE WHITE RAT. 1. HISTOLOGIC STUDY. (Fr.) Driessens, J. (Lab. Exp. Med., Inst. Cancer Res., Lille, France), A. Clay, J. Vanlerenberghe and L. Adenis. *C. R. Soc. Biol. (Paris)* 156(6):1099-1102, 1962.

Trypan blue (1%, 1 ml, s.c., every 15 days) in adult Wistar rats, given either until death (2-15 mo.) or until s.c. tumor formation (7-18 mo.) resulted in the development of malignant s.c. tumors in 22/35 (62%); 4 other rats showed very large multinodular liver tumors. Spleens were very much enlarged; there were no metastases. In a separate experiment after a minimum of 8 injections over 4 mo., s.c. tumors were produced in 14/40 (35%) rats, which appeared at least 10 mo. after the beginning of the injections. Three others had liver tumors. Microscopically, all the tumors showed malignant sarcomatous cellular proliferation, with irregularly distributed very large round cells, with eosinophilic cytoplasm, enormous teratologic nuclei, frequently multiple and polymorphic. Tumor-bearing rats survived usually about 1 mo. and showed no metastases. The tumors were probably histiocytosarcomas.

- 63-235 THE SIGNIFICANCE OF MOUSE SKIN TESTS OF CIGARETTE SMOKE CONDENSATE. (E.) Bock, F. G. and G. E. Moore. Pp. 72-86 in *Tobacco and Health*. James, G. and T. Rosenthal (Eds.). Springfield, Charles C. Thomas, 1962.

In a review of the literature (28 references) and some personal findings, the authors attempt to answer 3 objections often raised concerning the relevancy of mouse skin tests as a measure of the danger of smoking. In regard to smoking machine tar versus that in cigarette smoke, tars of similar potency have been obtained with analytical smoking machines and with manifold machines, operating with a wide range of variations in puff volume, duration and frequency, suction characteristics, burning temperature and final butt length; the type of machine is therefore not critical. The method of application also seems to have little effect, since similar tumor incidences were obtained from tar application in mice subjected to either repeated shaving with electric clippers at various intervals, sandpapering before each painting, or no trauma at all. In regard to the questioned similarity in response of mouse skin and the human lung, the authors report studies in mice showing an increase in tumorigenic effect of cigarette tar as a result of the removal of polar materials, the heptane-soluble fraction being more potent than the whole tar, while the benzene eluate of the heptane-soluble fraction (containing essentially no phenolic or acidic components), was about half as potent; this indicates that the tumorigenic activity is due to polycyclic hydrocarbons, which are known to produce tumors in human epithelial tissue. Work is reviewed which shows that the skin is not an unusually sensitive tissue and that species differences in susceptibility to carcino-

genesis are probably due to anatomical factors (skin thickness, penetrability and hair growth) rather than biochemical factors. It is concluded that a valid comparison of the responses of the target cells in different species is still impossible, so that studies with mouse skin are worth continuing.

- 63-236 SMOKING AND ORAL CANCER. (E.) Salley, J. J. (Dept. Oral Path., Med. Coll. Va., Richmond). *J. Dent. Res.* 42(1)(Pt. 2):328-339, 1963.

Daily applications of whole cigarette smoke to the ears and lips of Swiss and C57 mice or to the palatal mucosa of hamsters for periods up to 24 mo. produced no neoplastic changes. The ears of the mice did show some dyskeratotic changes, especially in the presence of vitamin B deficiency, which could be prevented during short periods of exposure by previous gonadectomy. Cigarette smoke also did not increase the number of ear malignancies produced in CAF₁ mice by daily UV irradiation (3/40 after 74 wk. UV alone, 5/40, after 78 wk.). In comparison, 3,4-benzpyrene (BP; 0.5% in acetone 3 x/wk., topically) + UV induced tumors in 32/40 after 18 wk. (BP alone, 33/40, after 25 wk.). No lip lesions were produced. In the cheek pouch, palatal mucosa or ear of the hamster, however, although cigarette smoke alone for periods of 64-86 wk. had essentially no effect, after a single application of 9,10-dimethyl-1,2-benzanthracene (DMBA), repeated application of tobacco smoke produced 3 cases of carcinoma, 8 of dyskeratosis and 31 of hyperplasia. Repeated applications of croton oil after the DMBA produced 6 cases of carcinoma, 11 of dyskeratosis and 31 of hyperplasia; all sites were represented. Finally, daily exposure of the hamster cheek pouch to cigarette smoke following 3 applications of DMBA resulted in carcinomas in 12/23 survivors with a latent period of 24 wk. (DMBA alone, carcinomas in 4/13 survivors, with a latent period of 38 wk.). The author therefore postulates that smoke is a cancer-promoting agent which, by means of a chronic irritant effect, favors the further malignant development of a latent malignant cell (due to a chemical, physical or viral carcinogen).

- 63-237 ENVIRONMENTAL FACTORS AND LUNG CANCER. (E.) Kotin, P. Pp. 244-263 in *Tobacco and Health*. James, G. and T. Rosenthal (Eds.). Springfield, Charles C. Thomas, 1962.

After pointing out some of the statistical problems in relating the incidence of lung cancer to any one environmental factor, be it smoking, air pollution or occupation, with particular attention to the fact that lung cancer develops in only 10-15% of heavy smokers and that there is no clear relationship between non-specific squamous metaplasia (detectable in the tracheae of most smokers and the eventual development of a neoplasm, the author concludes that cigarette smoke, by virtue of its irritant properties and its attenuating

effect on the respiratory epithelial defenses, provides a local environment which favors the action of a variety of carcinogens, whatever their source. He then discusses the endogenous factors determining the ultimate effect of the carcinogens in the environment. These factors include the histopathological pattern, the duration of exposure, the stability of environmental carcinogens and their concentration at the level of the respiratory tract, the relationship between particle size and the extent of pulmonary retention, the effect of the vehicle on the quantitative entry of the carcinogen into the host cell, the effect of cocarcinogens and anticarcinogens which may also be present in polluted air, the effect of irritants on the respiratory epithelium, ciliary activity and mucous secretion, and the significance of prior or coexisting pulmonary or systemic disease. The general conclusion to be drawn is that multiple factors are concerned with the initiation and promotion of lung cancer and that the abolition of smoking would not necessarily bring about a significant reduction in incidence.

63-238 ORGANIC PEROXIDES, HYDROGEN PEROXIDE, EPOXIDES, AND NEOPLASIA. (E.) Kotin, P. (Carcinogenesis Studies Branch, NCI, Bethesda) and H. L. Falk. *Radiat. Res.* (Suppl. 3):193-211, 1963.

On the basis of preliminary data from routine bioassays of the carcinogenic activity of a broad spectrum of organic peroxides and epoxides in mice, as well as an extensive review of the literature, the authors conclude that organic peroxides have a definite carcinogenic and radiomimetic effect, possibly ascribable primarily to catalysis of the depolymerization of DNA and RNA, and that this may be the mechanism of the mutagenic and carcinogenic effects of ionizing radiation. They also make a general assessment of the environmental status and carcinogenic role of various types of peroxides and epoxides in nature, attempting to relate their assay studies to the implied role of environmental carcinogens in the etiology of gastrointestinal and respiratory neoplasms. For example, in view of the possible carcinogenic effects of heated cooking fats, several lipoperoxides and epoxidated fats were tested in C57 mice. Epoxidated soya oil and butyl-9,10-epoxystearate, in groups of 50 mice each, were found to produce s.c. sarcomas, pulmonary adenomas and Hodgkin's disease in 3-10% (17-24 mo. latent period). Similarly, in view of the problem of air pollution, aerosol condensate from Los Angeles was tested and found to produce skin tumors in 20% of mice after topical application; significant numbers of pulmonary tumors were produced in inhalation experiments with ozonized gasoline (9.6%; controls, 1.6%), and epoxides presumably found in polluted air are currently being tested. The epoxides of cyclohexene, styrene, octylene, dodecene, hexadecene and epichlorhydrin, which are of industrial significance, were found to be somewhat carcinogenic in other

tests in groups of 50 mice: Hodgkin's disease occurred in 6-23% from all but cyclohexene epoxide (the latter produced 5% pulmonary adenomas). A large number of diepoxides was also tested and found to produce Hodgkin's disease and/or skin tumors in C57 mice. The authors then discuss some of the factors (antioxidants) which may modify the peroxide effect *in vivo*, and suggest that the radiomimetic effects of peroxides may be related to their susceptibility to destruction by catalase. Finally, the inconsistent relationship found between mutagenicity and carcinogenicity in many organic peroxides is pointed out, and further work on the relationship between carcinolytic and carcinogenic effects is recommended.

63-239 HISTOCHEMICAL OBSERVATION ON EXPERIMENTAL TUMORS INDUCED BY SUBCUTANEOUS ADMINISTRATION OF CARCINOGENIC HYDROCARBONS. (E.) Okamoto, Y. (Dept. Oral Surg., Osaka U. Dent. Sch., Japan), I. Murata, T. Miyaji and H. Kawashima. *Gann* 54(1):39-46, 1963.

Single injections of 0.5 ml of 0.5% solutions of 9,10-dimethyl-1,2-benzanthracene, 3,4-benzpyrene, 5,6-dibenzanthracene or 20-methylcholanthrene in acetone into mice induced a mixture of spindle-cell, fibro-, polymorphocellular, osteogenic, giant cell and mixed sarcomas, often with several histological types in a single tumor, and with no demonstrable relationship between the carcinogen used and tumor type obtained. Histochemical studies also revealed no differences among the carcinogens. Generally, alkaline phosphatase was absent from tumor tissue, and other enzymes were low, but succinic dehydrogenase, β -esterase and β -glucuronidase activities were high, especially in giant cells. Acid phosphatase, β -esterase and β -glucuronidase activities were also high in cells lining the walls of cysts.

63-240 NEOPLASIA: LUNGS. (E.) Passey, R. D. Pp. 105-122 in *Tobacco and Health*. James, G and T. Rosenthal (Eds.). Springfield, Charles C. Thomas, 1962.

The author presents some of the statistical findings with respect to the incidence of lung cancer which have convinced him that this disease is not caused by inhalation of carcinogens but is the sequel to chronic tissue damage of a nonspecific nature, such as respiratory lesions established by infection or chronic catarrh, bronchitis, tuberculosis, bronchiectasis, pulmonary abscess, pneumonia or pleurisy, or the damage produced by tobacco or other smoke or industrial air pollution. He points out that the squamous epithelium of the oral cavity should be more susceptible to carcinogens in tobacco smoke than the columnar epithelium of the bronchi, but that the latter is more susceptible to nonspecific irritants. Moreover, there are more carcinogens in the smoke from pipes or cigars than in cigarette smoke, but the latter is more acidic and irritating. There also seems to be no correlation between the exposure to tobacco smoke

and the onset of lung cancer, the average age of onset being about 57 yr. regardless of smoking history, while in cancers due to carcinogens (bladder cancer, chimney sweeps' cancer, lung cancer in Schneeberg miners) the duration of exposure has a clear effect. Some of the positive correlations between chronic respiratory tract inflammation and lung cancer are also pointed out. Therefore, instead of attempting to remove carcinogens, cigarettes should simply be made less irritating, and all respiratory diseases must be treated early. Finally, the author mentions experiments showing that the wt. loss due to smoking is not caused merely by a lower food consumption but by an alteration in protein metabolism, increasing the danger for the growing organism.

63-241 PROBLEMS IN THE ASSAY OF CARCINOGENS. (E.) Blum, H. F. (NCI, Bethesda). Nat. Cancer Inst. Monogr. (10):639-647, 1963.

In a general discussion of the difficulties in the quantitative bioassay of carcinogenic activity, based mainly on his previously published work, the author uses the example of cutaneous carcinogenesis by ultraviolet radiation to illustrate the variability in development time (latent period), the effect of discontinuation of treatment, and the dose-response relationships; even if a quantitative model can be set up for experimental animals, extrapolation of such results to man is not feasible because of differences in skin thickness and penetrability. Finally, even more difficult problems are presented by chemical carcinogenesis since absorption, metabolism and distribution in the body play a role and have a marked effect on the dose-response relationships. Since no unifying quantitative model can be set up, assay results are largely unreliable and the setting of human tolerance levels to carcinogenic agents is considered inadvisable.

63-242 PULMONARY LESIONS IN DOGS FROM METHYLCHOLANTHRENE. (E.) Rigdon, R. H. (Dept. Anesthesiol., U. Mich. Med. Ctr., Ann Arbor)

and G. Corssen. Arch. Path. 75(3):323-331, 1963.

Intrabronchial injections of 20-methylcholanthrene (20-Me) in either polysorbate 80 or sodium dipropyltrizoate + diatrizoate (Ditriokon) were given to 19 anesthetized female mongrel dogs, while 5 others received the solvents alone; postmortem examinations revealed bronchial epithelial metaplasia 18-36 days after administration of 125-240 mg of 20-Me in 3 dogs (in 1, a local area was infiltrated with squamous epithelium, but there were no metastases). Since there were no lesions in the 4 dogs surviving the longest after 20-Me, and since hyperplasia was also found in controls, no definite relationship could be established between the lesions and the carcinogen. 20-Me produced mechanical obstruction of the bronchi and inflammatory changes leading to acute pulmonary edema and, in many cases, pneumonia; however, similar symptoms were produced by injection of the solvents alone, and chronic pneumonitis also occurred spontaneously in controls.

63-243 AN EARLY TEST FOR POSSIBLE SKIN CARCINOGENS. (E.) Iversen, O. H. (Inst. Gen. Exp. Path., U. Oslo, Norway). Nat. Cancer Inst. Monogr. (10):633-637, 1963.

A study of the activity of the energy-generating processes by the tetrazolium reduction method revealed increased deposition of formazan in hairless mouse epidermis the first 2 days after a single application of either 1% 20-methylcholanthrene, 0.5% 9,10-dimethyl-1,2-benzanthracene, 0.16% 3,4,9,10-dibenzpyrene or 0.5% croton oil (all in benzene), while application of noncarcinogens such as benzene, urethan, phenanthrene and 1,2-benzanthracene was followed by a decrease in formazan deposition. The initial increased deposition following carcinogens was also followed by a prolonged decrease. Further studies of 21 compounds (7 carcinogens and 14 noncarcinogens, in benzene, 1% or 3.73×10^{-2} M), showed complete correlation between carcinogenic activity and increased deposition of formazan. This test, the mechanism of which is unclear, may be useful in screening compounds for carcinogenic activity.

See also abstract nos.: 147, 148, 150, 159, 160, 161, 166, 172, 178, 273, 296

VIRAL CARCINOGENESIS

- 63-244 POSSIBILITIES OF USING SEROLOGIC METHODS IN CARCINOLOGIC RESEARCH. (Fr.)
 Illinger, E. (Pasteur Inst., Tunis, Tunisia).
Ann. Inst. Pasteur Med. 40(4):459-463, 1962.

Antiserum to vaccinia virus grown on heifer kidney neutralized (per minute) 20% of the heifer kidney-grown virus, but only 10% of vaccinia virus grown on KB cells, and 5.6% of the virus grown on chick chorioallantoic membrane. The authors hypothesize that common DNA viruses, such as adenovirus or pox viruses may incorporate "oncogenicity" on passage through a cancerous host, and that the change may be detectable by serologic methods.

- 63-245 THE VIRAL THEORY OF CANCER (ON THE BASIS OF ELECTRON MICROSCOPY). (It.)
 Bernhard, W. (Gustave Roussy Cancer Inst., Villejuif, France). *Gazz. Sanit.* 33(10-11):1-585, 1962.

In an address before a symposium on "Cellular changes due to chemical, physical and viral agents", held in Milan, Italy on June 17, 1961, the author reviews the morphology of virus infections, the fundamental structure of viruses, the relationships between the virus and the host cell, and the nuclear, cytoplasmic and extracellular lesions produced by viruses. He concludes with a brief review of the evidence favoring a viral etiology for certain human tumors and illustrating (with electron microscopy, photographs) cellular lesions produced by the polyoma and chickenpox viruses which are similar to those observed in Hodgkin's disease.

- 63-246 THE CHEMICAL COMPOSITION OF LEUKEMIC LEUKOCYTES OF VIRUS-INDUCED LEUKEMIA. (Ger.) Bieleka, H. (Inst. Exp. Cancer Res., Ger. Acad. Sci., Berlin-Buch) and I. Schneiders.
Acta Biol. Med. German. 9(5):445-457, 1962.

The acid soluble P content of leukocytes from lymph nodes and thymus of leukemic mice (virus-induced or transplanted from virus-induced leukemia) was significantly higher than in comparable normal tissues. The phospholipid content of virus induced lymphoid leukemia leukocytes (3.4% by dry weight) was much higher than in normal controls (spleen and bone marrow cells); myeloid leukemia leukocytes and in transplanted leukemia leukocytes, however, it was not increased (%). In all types of leukemic leukocytes, the DNA content of the individual cell was 1.5 to 3 times higher than in control cells; in terms of dry weight compared to bone marrow, however, this increase was apparent only in the case of virus-induced lymphoid and transplanted myeloid leukemia. Compared to spleen, all showed increase in RNA. In virus-induced myeloid leukemia leukocytes, the DNA content per cell was far higher than in transplanted myeloid, lymphatic cells or

controls. In terms of dry weight all values were lower compared to bone marrow and higher compared to normal spleen, although values for lymphoid cells were only slightly increased. DNA content/lymphoid cell did not differ from that of spleen. The DNA content, a function of the number of chromosomes, was dependent on the maturity of the leukocyte. The different DNA/RNA ratios in the leukocytes of different types of leukemia reflected differences in the nucleus/plasma ratio. The protein content of leukemic leukocytes ranged from 60-68% of dry weight and thus did not differ appreciably from that of various normal tissues.

- 63-247 BIOCHEMICAL DIFFERENTIATION BETWEEN MYELOID AND LYMPHATIC LEUKOCYTES IN CASES OF VIRAL LEUKEMIA. (Ger.) Bieleka, H. (Inst. Exp. Cancer Res., Ger. Acad. Sci., Berlin-Buch). *Acta Biol. Med. German.* 9(5):585-593, 1962.

Comparative biochemical studies on leukocytes from the lymph nodes and thymus of mice with virus-induced myeloid or lymphatic leukemia showed that lymphoid leukemia leukocytes (LLL) have a lower endogenous respiration in the absence of phosphate than myeloid leukemia leukocytes (MLL), but a higher content of acid-soluble phosphate and phospholipids. In the absence of phosphate, MLL show a Crabtree effect while LLL do not, glucose being stimulatory. The DNA content is higher in MLL, while the RNA content is higher in LLL and the respective RNA/DNA ratios are 0.55 and 0.9. The RNA from MLL has a higher content of adenylic acid and a lower content of cytidylic acid than the RNA from LLL. Otherwise, the 2 types of leukemic cells were essentially the same. (See also CRA 1(2):#246, 1963.)

- 63-248 SUDDEN MANIFESTATION OF PRONOUNCED ONCOGENIC ACTION IN A LINE OF LONG-AVIRULENT POLYOMA VIRUS. (Ger.) Graffi, A. (Inst. Exp. Cancer Res., Ger. Acad. Sci., Berlin-Buch), J. Gimmy and L. Baumbach. *Acta Biol. Med. German.* 9(5):553-556, 1962.

While 2 previously isolated substrains of polyoma virus (BB/T2 and BB/T3) from embryo cultures of mouse chloroleukemia showed similar cytopathogenic effect *in vitro*, only the T2 line produced tumors; the T3 line was completely negative in rats, hamsters, mice, and guinea pigs through 32 passages on mouse embryo tissue. However, nutrient solution from the 33rd passage of this apparently avirulent line suddenly became highly virulent, producing a new and peculiar pathologic picture in 5/12 surviving mice. After a latent period of 106-203 days, multiple cysts (some filled with hyaline cylinders), appeared in the kidneys, and numerous nodes were found in the mesentery of the small intestine. While these changes were degenerative, rather than proliferative, re-isolation of this virus line led to the acquisition of a potent oncogenic action, with multiple tumor

development after 4-6 wk. in about 70% of treated rats and, somewhat later, in 60% of infected mice. In rats, the tumors were sarcomas of the bones and kidneys; in mice, parotid and mesenchymal tumors. Simultaneously, the cystic kidney degeneration and mesenteric vessel changes induced after passage 33 disappeared and were later observed only in isolated cases. No such change in the tumor spectrum was observed in the case of rats.

- 63-249 PURIFICATION OF POLYOMA VIRUS. (E.) Winocour, E. (Div. Biol., Calif. Inst. Tech., Pasadena, Calif.). Virology 19(2):158-168, 1963.

A method of virus purification is described based on the use of high-titer polyoma virus pools, produced in kidney cultures derived from infected suckling mice, which are then concentrated by sedimentation and purified by equilibrium centrifugation in a cesium chloride density gradient. Data on the homogeneity of the purified virus preparations, obtained by studies in the ultracentrifuge, are presented. Equilibrium centrifugation in a cesium chloride density gradient fractionates crude polyoma virus into 2 main bands. A fraction at density 1.339 g/ml displayed infectivity comparable to its hemagglutinating activity, an UV absorption spectrum typical of a nucleoprotein, and consisted mainly of "full" particles in the electron microscope. The virus concentrated at 1.297 g/ml showed hemagglutinating activity without corresponding infectivity, a typical protein-like UV spectrum, and had the appearance of "empty" particles. From the differences in buoyant densities, it was estimated that the "full" particles contained 13.4% DNA.

- 63-250 THE SUBVIRAL INFECTIVE AGENT FROM POLYOMA VIRUS. (E.) Weil, R. (Div. Biol., Calif. Inst. Tech., Pasadena). Pp. 83-87 in Basic Mechanisms in Animal Virus Biology. V. 27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

The subviral infective agent (SIA) from polyoma virus, extracted from infected mouse embryo tissue cultures or from purified polyoma virus, although it contained the genetic information for the replication of polyoma virus, and was sensitive to pancreatic DNase, the SIA was unusually heat-stable. Phenol extracts containing SIA, after heating to 100°C for 4 and 8 min. contained 5.9 and 5.0×10^3 plaque forming units (pfu)/ml; unheated control contained 1.8×10^3 pfu/ml. Inactivation of SIA with formaldehyde (1.8%) was very slow, but after heat denaturation, its sensitivity to formaldehyde increased and was rapidly inactivated to a survival of about 5%; the residual infectivity probably represented largely renatured SIA. In a CsCl density gradient, the heat-denatured SIA formed two separate bands of about equal infectivity: one which had the density

of denatured polyoma DNA was rapidly inactivated by formaldehyde while the other, of "largely renatured" SIA, was not affected by such treatment. Treatment with formamide did not affect the infectivity of SIA, and even permitted a moderate increase of infectivity, whereas other DNA (of viral, bacterial, or of mammalian origin) was denatured. It is suggested that the SIA was indeed denatured, but that it renatured during centrifugation in the CsCl gradient. At pH 3 or lower, SIA rapidly lost infectivity, probably because of increased depurination following denaturation. The unusual tendency of polyoma DNA and the SIA to renature after heat denaturation is not understood.

- 63-251 THE DENATURATION AND THE RENATURATION OF THE DNA OF POLYOMA VIRUS. (E.) Weil, R. (Div. Biol., Calif. Inst. Technol., Pasadena). Proc. Nat. Acad. Sci. USA 49(4):480-487, 1963.

Essentially the same material as reported in the preceding abstract, but with more procedural detail.

- 63-252 ANTIVIRAL AND ANTITUMOR IMMUNOLOGIC MECHANISMS OPERATIVE IN THE SHOPE PAPILLOMA-CARCINOMA SYSTEM. (E.) Evans, C. A., (Dept. Microbiol., U. Wash., Seattle), R. S. Weiser and Y. Ito. Pp. 453-462 in Basic Mechanisms in Animal Virus Biology. V. 27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

Standardized, multiple applications to 58 young rabbits of Shope papilloma virus (approximately 100 times more concentrated than the minimally infective dilution) onto an abraded area of skin 12 mm in diameter, resulted in tumors in all which were identifiable in 21 days; 23 with both large and small tumors, and 6 with only small tumors showed spontaneous regression. Regressions occurred more often in small tumors (11/23) than in large (2/22). Virus concentration of the inoculum (10% or 1%) did not affect regression rate. Injection of serum from rabbits with long-persistent papillomas or of "hyperimmune" serum (20 ml/wk. x 5, 7 days after virus inoculation or 30 ml plus 8 ml/wk. x 2 or 3, 19 days after virus inoculation) from donors which had been previously inoculated repeatedly with a 20% suspension of cottontail papilloma tissue did not prevent or diminish tumor regression. Attempts to promote regression were equally futile. Serum from donors whose papillomas had regressed completely (30 ml/day x 3, i.p., starting 16 days after virus inoculation), did not increase tumor regression in recipients, nor did it change the time of regression. It is concluded that tumor regression probably is not mediated by any kind of circulating (humoral) antibody. Attempted transfer of regression immunity by "immune" cells from lymph nodes ($1.3-12.0 \times 10^6$) and spleens ($11-51 \times 10^6$) of rabbits undergoing papilloma regression also failed. Vaccines of crude extracts of cottontail papillomas (1% and 20%) injected intracutaneously (0.1-0.2 ml

ml at 6 sites) increased regression rate 71% and 79%, resp. Semipurified virus vaccine also stimulated tumor regression (67%). Similarly, intradermal injection of minced domestic rabbit papilloma, with its cell viability resulted in tumor regression in 73% of 86 rabbits (17% of 29 controls). Ineffective were attempts to suppress vaccination-stimulated (immunologic) regression by treatment with antigen (supernatant of centrifuged 10% tumor suspension); by cortisone acetate and by excision of popliteal lymph nodes which drained the tumor-bearing feet. The evidence adduced favors the concept of cell-associated immunity.

- 63-253 BEHAVIOR OF SOME ENZYME ACTIVITIES OF SPLEEN TISSUE IN EXPERIMENTAL FRIEND'S LEUKEMIA. (It.) Di Simone, A. (Inst. Spec. Med., Path. U. Naples, Italy), G. Budillon, A. M. Barbieri, C. Del Vecchio-Blanco and F. Cocco. Boll. Soc. Ital. Biol. Sper. 38(20):1026-1027, 1962.

Friend's leukemia was induced in mice by the inoculation of leukemic tissue and the hexokinase, phosphofructokinase, glyceraldehyde-3-P-dehydrogenase, 3-phosphoglyceric kinase, enolase, pyruvic kinase, and creatine-phosphokinase activity of spleen homogenates was determined. Only the 3-phosphoglyceric kinase level showed a marked increase in all phases of the disease, beginning with day 5, when it was 7.48 (μ M substrate utilized/mg protein in 5 min. at 37°), as against 4.98 in controls. Other enzymes undergoing less pronounced but statistically significant changes were creatine-phosphokinase (reduced on day 5 only), and glyceraldehyde-3-P-dehydrogenase, which increased in the later stages. The increase in 3-phosphoglyceric kinase activity may allow increased utilization of energy produced from glycolysis. The fact that the enzyme changes observed in Friend's leukemia are different from those found in other leukemias suggests that the metabolic picture in various malignant hemopathies is not a uniform one.

- 63-254 ANAEROBIC GLYCOLYSIS IN SPLEEN TISSUE IN VARIOUS PHASES OF EXPERIMENTAL FRIEND'S LEUKEMIA. (It.) Budillon, G. (Inst. Spec. Med., Path. U. Naples, Italy), A. Di Simone, C. Del Vecchio-Blanco, A. M. Barbieri and F. Cocco. Boll. Soc. Ital. Biol. Sper. 38(20):1024-1025, 1962.

Swiss mice were inoculated i.p. with 0.1 ml of a 10% cell-free extract of leukemic spleen tissue, when sacrificed at various intervals, only in the early stage of the disease (day 5) was the glycolytic activity of spleen tissue from experimental animals decidedly higher than in normal controls: 89.80 μ l CO₂/10 mg protein/15 min. at 37° C, as against 64.02 in control spleen tissue. This early and transient metabolic change is attributed to virus multiplication, rather than to malignant cell proliferation.

- 63-255 ALTERATION OF SERUM LACTIC DEHYDROGENASE ACTIVITY AFTER INFECTION WITH MOUSE TUMOR VIRUS AS A DISTURBANCE OF REGULATION IN VIVO. (Ger.) Georgii, A. (Path. Inst., Ludwig-Maximilians U. Munich, Germany). Verh. Deut. Ges. Path. 46:357-358, 1962.

After injection of cell-free filtrates of mouse sarcoma Sa. 1 (which induces myeloid leukemia), increased serum lactic dehydrogenase (LDH) activity was observed on day 2; it reached a maximum (8-10 x normal level) on day 7 and remained high (5 x normal level) thereafter for over 140 days. After similar injections in newborn animals, increased LDH activity persisted throughout the animals' lifetime. No histological changes were seen which could be correlated with the alteration in enzyme activity. This "LDH effect" could be transmitted from animal to animal, and was not reduced by dilutions to about 10⁻⁶, indicating that the agent responsible was an LDH-active virus present in the mouse sarcoma. Similar results were obtained with Ehrlich ascites tumor; the LDH-active virus could not be isolated from spontaneous mouse tumors. Injection of cell-free filtrates of so-called LDH-activating tumor transplants also induced myeloid leukemia in 40% of "baby" mice 10 mo. later and increased serum LDH in all; cell-free extracts of leukemic tissue also produced a 6-8-fold rise in serum LDH in normal mice, as did virus isolated from a mouse myeloid leukemia tissue culture. The LDH effect is specific to certain tumor viruses: it is not produced by poliomyelitis virus, for example, and only occasionally by polyoma virus. The LDH effect reflects a permanent alteration of cellular metabolism and makes it possible to detect virus-invaded host cells. See also CRA 1(1):#67, 1963.

- 63-256 GEL FILTRATION OF SE POLYOMA VIRUS HAEMAGGLUTININ ON SEPHADEX. (E.) Jonsen, J. (Dept. Virol., Nat. Inst. Pub. Health, Oslo, Norway), K. Helgeland and O. Lahelle. Acta Path. Microbiol. Scand. 56(4):421-425, 1962.

Data are presented for the recovery of virus hemagglutinin during the elution of SE polyoma virus from columns of the crosslinked polysaccharide dextran Sephadex G 75 by means of phosphate buffer (0.01 M at pH 5.5, 6.0, 6.5 and 7.2; 0.001 M at pH 7.2). There was little difference between the buffers, and no evidence that the hemagglutinins were separated into fractions with different affinities for the dextran. The technique is recommended for the desalting of virus suspensions in nutrient media.

- 63-257 VARIATION IN INTERFERON PRODUCTION BY POLYOMA VIRUS STRAINS OF DIFFERING ONCOGENICITY. (E.) Friedman, R. M. (NIH, Bethesda), A. S. Rabson and W. R. Kirkham. Proc. Soc. Exp. Biol. Med. 112(2):347-349, 1963.

A comparison of interferon production in mouse embryo fibroblast (ME-29 cells) cultures infected

with either the highly oncogenic S variant or the poorly oncogenic M variant of polyoma virus showed that infection with the M variant led to 4-8 times higher titers of interferon, while the S variant produced higher titers of virus. These results are probably related to the larger plaque size of polyoma virus variants of higher oncogenicity, but are not responsible for the differences in susceptibility of different mouse strains.

63-258 FURTHER STUDIES ON THE RELATIONSHIP BETWEEN THE EFFECT OF MOUSE MYELOID LEUKEMIA VIRUS AND VARIOUS BIOLOGICAL CONDITIONS IN THE INFECTED ANIMALS. (Ger.) Kruschke, W. (Inst. Med. Biol., Ger. Acad. Sci., Berlin-Buch) and A. Graffi. *Arch. Geschwulstforsch.* 20(1): 22-29, 1962.

Experiments with various strains (C57, CBA, XVII (Paris), A, AB, sg, db) of newborn mice inoculated s.c. with the virus of mouse myeloid leukemia (cell-free filtrates of lymph node, thymus and spleen of leukemic mice) revealed no significant changes in either the percentage of mice infected (average for 7 strains: male 72%, female 79%) or the latent period in response to: the sex of the animal; administration of additional sex hormones (testosterone propionate (40 mg, i.m.) or diene-estrol acetate (1.5 mg) between the 5th and 7th wk. of life); the strain of mouse (although the average latent period varied from 120 days in C57 mice (80% leukemic) to 228 days in db mice (44% leukemic) strain A, with a small number of animals, showed about 15% leukemia and average latent period of 130 days; variations in diet (oats, concentrated food pellets, oats with egg yolk or with egg white, leukemia ranged between 62%-73%, average latent period between 86-165 days); administration of vitamin B₁₂ (10-15 µg x 2/wk. s.c. for 5 mo. beginning 1 day after filtrate injection, total dose 500-600 µg), or blocking of the reticuloendothelial system by administration of Trypan Blue (0.2 ml of 0.2% saline solution, first injection 24 hr. prior to virus infection, 2nd injection 18 days later). As a result of the last 2 treatments, the number of mice infected was somewhat reduced (26% and about 29%, resp., as compared to about 46% and 50% in controls); also the latent period was shortened (100 days and 120 days, resp., controls 125 days and 142 days, resp.). Thus, in contrast to other mouse leukemias, the effect of myeloid leukemia virus seems to be independent of the biological characteristics of the host.

63-259 CYTOLOGIC AND VIROLOGIC STUDIES OF CULTURES DERIVED FROM NEOPLASTIC AND NON-NEOPLASTIC TISSUES OF CHILDREN. (E.) McAllister, R. M. (Dept. Pediat., U. So. Calif. Med. Sch., Los Angeles), M. Mikenas, R. M. Straw and B. H. Landing. *Lab. Invest.* 12(3):343-354, 1963.

In an attempt to detect viruses in abnormal human tissues by long-term culture of small biopsy

specimens, minced fragments of various tissues were incubated in Eagle's medium supplemented with 20% inactivated calf serum, 5% human cord serum, 5% beef embryo extract and antibiotics. Cells were cultivated from 59/67 neoplastic tissues (mostly nervous system tumors and lymphomas); 45/51 non-neoplastic abnormal; and from 26/32 normal tissues: these cultures could be maintained by serial subcultivation for 1-48 passages. There were no significant differences in apparent rate of metabolism or length of survival *in vitro* between neoplastic and non-neoplastic tissues and none became permanent cell lines. There were no cytologic abnormalities in 77 cultures (25 neoplastic, 27 non-neoplastic abnormal and 25 normal). Cultures of 6 of 13 specimens of hypertrophied tonsils developed cytopathic effects and intranuclear inclusions, and eventually yielded adenoviruses. These 6 cultures, as well as 3 other tonsil specimens, showed polykaryocytes. No other viruses were isolated, but polykaryocytes were found in a total of 33 neoplastic, 17 non-neoplastic abnormal, and only 1 normal tissue (thymus). Although in some cultures these polykaryocytes appeared similar to cells present in the tissues *in vivo*, in other cultures, particularly those derived from neural tumors, they appeared to represent new cytologic characteristics. The significance of these polykaryocytes is unclear. While the possibility of still additional unmasked viruses is suggested, their clear demonstration remains unaccomplished.

63-260 EFFECT OF A CHELATING AGENT ON THE COURSE OF EXPERIMENTAL INFECTION BY CERTAIN VIRUSES, AS WELL AS ON THE DEVELOPMENT OF CERTAIN TUMORS: EHRLICH ASCITES CARCINOMA AND ROUS SARCOMA II. (Fr.) Balmuş, G. (Inst. Inframicrobiol., Acad. R.P.R., Bucharest) and I. Samuel. *Rev. Sci. Med. (Bucur.)* 7(3-4):135-138, 1962.

Treatment with Ca-EDTA-Na₂ inhibited both the development of MM virus infection in mice and the growth of Ehrlich ascites carcinoma in mice or Rous sarcoma in chicks, whereas the same agent stimulated the multiplication of influenza and of herpes virus in mice.

63-261 EVIDENCE OF CONTINUOUS TRANSMISSION OF NONINFECTIOUS SV 40 VIRAL GENOME IN MOST OR ALL SV 40 HAMSTER TUMOR CELLS. (E.) Sabin, A. B. (U. Cincinnati Coll. Med., Ohio) and M. A. Koch. *Proc. Nat. Acad. Sci. USA* 49(3):304-311, 1963.

SV 40 virus, in very small amounts was recovered irregularly and only from occasional SV 40 virus-induced tumors during 31 serial passages in adult hamsters. Tumors without virus could give rise to tumors with virus and vice versa. These hamsters had no neutralizing antibody; the tumor extracts contained no inhibitors for small amounts of SV 40 virus. In primary cultures, large number of tumor cells either failed to release virus or rarely did so in single bursts of minute amounts;

viral antigen could not be detected in the nuclei by the fluorescent antibody technic. Prolonged propagation and serial passage of tumor cells in tissue culture induced the release of larger, though still small, amounts of virus in previously virus-free cultures (12 mo. or more). Large amounts of SV 40 virus added to *in vitro* cultures of tumor cells failed to produce infectious virus. After transplantation of approximately 2 cells in adult hamsters, 9/12 of the resultant tumors yielded minute amounts of virus, indicating that most, and perhaps all, of the tumor cells carried the SV 40 viral genome in a noninfectious state and that maturation of the virus occurred only rarely in an occasional cell. The similarity between these findings and bacterial lysogeny requires further study.

63-262 THE IMMUNOLOGICAL BASIS FOR NON-INFECTIVE ROUS SARCOMAS. (E.) Rubin, H. (Virus Lab., U. Calif., Berkeley). Pp. 441-452 in Basic Mechanisms in Animal Virus Biology. V. 27 of the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.) Biol. Lab., Long Island Biol. Assn., 1962.

Rous sarcoma virus (RSV) content of 0.1 g of tumor homogenate declined from more than 10^6 focus-forming units (FFU) to less than 10^1 FFU 29 days after infection of control birds with 10^{-2} , 10^{-4} , and 10^{-6} dilutions of RSV. Chickens, rendered tolerant by infection with the immunologically indistinguishable Rous associated virus (RAV), after infection with RSV dilutions of 10^{-2} , 10^{-3} , and 10^{-4} , continued to yield more than 10^7 RSV per 0.1 g of tumor homogenate, with no decline in virus production, and a rise rather than decline of infectivity. The decline with age of tumor, in the infective virus content of RSV and the similar decline in virus producing capacity of intact cells, were found to be due to an immunological reaction by the host, which is mediated by immunologically competent (lymphocyte) cells rather than by circulating antibodies; the target of this reaction is the infected cell rather than the infective virus. The effect of these cells is to suppress virus synthesis rather than to neutralize virus. It must be assumed that a new antigen appears in the infected cell, which is then treated as is a foreign cell in the homograft reaction. This new antigen appears to be common to all Rous sarcomas. The reduction in virus yield with time is attributable to damage to the tumor cell by immunologically competent lymphocytes.

63-263 IN VITRO STUDIES ON POLYOMA VIRUS INFECTION, WITH SPECIAL REFERENCE TO DEOXYRIBONUCLEIC ACID SYNTHESIS AS DETERMINED BY AUTORADIOGRAPHY. (E.) Minowada, J. (Roswell Park Mem. Inst., Buffalo) and G. E. Moore. Gann 54(1):59-70, 1963.

Infection of secondary Swiss mouse embryo cultures (in medium 199 plus 20% calf serum) with polyoma virus led to a reproducible sequence of cytopatho-

genic effects (clumped, rounded cells with refractive cytoplasmic vacuoles and nuclear abnormalities) which paralleled the appearance of virus in the culture fluid and was followed, after a few wk., by the establishment of continuously-growing cells which eventually replaced the earlier degenerating cell population and was accompanied by a gradual decrease in virus production. Upon injection of these cells into young, X-irradiated mice, no tumors appeared at the site of inoculation, but parotid tumors were produced. Hence, the infected cells were of the "virus carrier" type rather than being "transformed" neoplastic cells. Autoradiographic, cytochemical and immunofluorescent studies of DNA synthesis in such infected mouse embryo cultures grown in the presence of tritiated thymidine showed that most of the increased DNA synthesis in infected cells could be accounted for by *de novo* synthesis of viral DNA. See also CRA 1(1):#112, 1963.

63-264 THE PHYSICAL CHARACTERISTICS OF POLYOMA VIRUS. II. THE NUCLEIC ACID. (E.) Crawford, L. V. (Dept. Virol., U. Glasgow, Scotland). Virology 19(3):279-282, 1963.

The extraction and characterization of polyoma virus DNA are described. Studies of the relation between temperature and UV absorption (melting curves), as well as density gradient centrifugation in CsCl and sedimentation velocity studies showed that polyoma virus DNA is a double-stranded molecule with a molecular weight of $2.2-17.6 \times 10^6$ and a base composition containing 48% guanine plus cytosine.

63-265 BIOPHYSICAL STUDIES ON THE NATURE OF THE SIMIAN PAPOVA VIRUS PARTICLE (VACUOLATING SV40 VIRUS). (E.) Mayor, H. D. (Dept. Virol., Baylor U. Coll. Med., Houston, Texas), R. M. Jamison and L. E. Jordan. Virology 19(3):359-366, 1963.

A detailed study of the physicochemical properties of simian papova virus, grown in monolayer cultures of trypsinized kidney epithelial cells from African green monkeys, showed that the virus particle has a diameter of 45 mμ and a CsCl buoyant density of 1.30. The complete virion has a molecular weight (MW) of 4.4×10^7 , of which 9% is double-stranded DNA (a minimum MW of 4×10^6 avograms of DNA per virus particle). The virus particle exhibits cubic symmetry, and the capsid is composed of 42 protein capsomers; each of the approximately 240 subunits of the capsid has a MW of about 167,000. Fluorochrome staining and photodynamic inactivation studies indicate that acridine orange is capable of penetrating the capsid and inhibiting the mature virion.

63-266 THE EFFECT OF ADENOVIRUS 3 ON HUMAN BRONCHIAL EPITHELIUM IN TISSUE CULTURE. (E.) Maddy, F. V. (Virus Div., Pasteur Inst., Paris). Ann. Inst. Pasteur (Paris) 104(1):43-48, 1963.

Tissue cultures of epithelial explants (modified Maximow double coverslip method) from normal biopsies of the human bronchus formed extensive sheets of epithelial cells within 7 days after implantation. Ciliary activity continued throughout. Addition of 0.1 ml of adenovirus 3 (10^{-3}) brought about cytopathogenic effects in 16 hr.: detachment from the sheet of dense epithelial cells, enlarged nuclei with rearranged chromatin, and prominent nucleoli. Cells of treated cultures as a whole showed more mitotic figures than the controls and stimulation of growth. Some ciliated cells showed basophilic and eosinophilic inclusions in the nucleus and cytoplasm. The adenovirus 3 destroyed the dedifferentiated growth of the HeLa, KB, and monkey kidney (control) cells in 3-4 days. Tissue cultures of bronchial aspirates, consisting of epithelial cells and fibroblasts, grew out in 24 hr. When treated with adenovirus they showed increased histiocytes and formation of syncytia; cellular activity and growth surpassed that of controls. If adenovirus 3 was added before growth began, only the virus-treated cells showed activity. Tissue cultures of malignant material, mostly aspirates, showed marked structural abnormalities; mitotic and phagocytic activity were increased. Malignant cultures treated with adenovirus 3 showed accentuated vacuolization of the cytoplasm, with nuclear displacement and marked phagocytosis.

- 63-267 PROPERTIES OF CELLS INFECTED WITH AVIAN MYELOBLASTOSIS VIRUS. (E.) Baluda, M. A. (City of Hope Med. Ctr., Duarte, Calif.). Pp. 415-425 in Basic Mechanisms in Animal Virus Biology. V. 27 of the Cold Spring Harbor Symposium on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

In an extensive review of his own previously published work with avian myeloblastosis virus (AMV), the author discusses the history and general characteristics of the virus, its pleotropic nature, the in vivo effects of AMV in chick embryos and adult chicks, the possibility of oncogenic conversion of the cells in vitro and the nature of the converted cells, the nature of the target cells which are susceptible to conversion, the effects of AMV on various types of tissue in vitro, and the production of virus by infected cells. AMV can infect all types of chicken cells, either embryonic or adult, and can produce 4 main

categories of leukosis: acute leukemia, visceral lymphomatosis, kidney tumors and osteopetrosis. Every infected cell becomes a virus yielder, but oncogenic conversion is limited to specific target cells both in vivo and in vitro; after infection, these target cells proliferate and differentiate, up to a certain point, in their normal sequence of development. The morphology and fate of the converted cell is described in considerable detail and the problem of spontaneous recovery from viral leukemia is discussed, as are the reasons for the changes in tumor resistance with age of the host. (26 references)

- 63-268 A VIRUS-INDUCED TUMOR IN PRIMATES. (E.) Ambrus, J. L. (Roswell Park Mem. Inst., Buffalo), E. T. Feltz, J. T. Grace, Jr. and G. Owens. Nat. Cancer Inst. Monogr. (10):447-459, 1963.

Homogenates from lesions in the rhesus monkey which were induced by the Yaba virus, injected s.c. into rhesus or cynomolgus monkeys, produced 100% takes; in the pigtail macaque 1/2 developed a lesion, as also occurred in 2/6 African green monkeys (after a long latent period); other African and South American monkeys were not susceptible. Cell-free filtrates also induced 80%-100% takes in rhesus and cynomolgus monkeys. Dogs, rabbits, guinea pigs, hamsters, and rats were not susceptible by any route of administration. In man and monkey, infection was only by inoculation, not by contact. Human lesions (1 accidentally inoculated technician, 5 volunteer cancer pts.) were indistinguishable from those of monkeys (histiocytomas) and were transplantable to both primates alike. Inoculations were effective at dilutions of up to 10^{-6} ; some animals developed permanent immunity after recovery, in others, the tumors finally regressed, but secondary tumors developed in distant areas, in some cases going through 3 to 5 infectious cycles. The tumors, consisted of enlarged, transformed histiocytes. No malignant transformation occurred on treatment with 20-methylcholanthrene or dibenzanthracene; some lesions of monkeys so treated even regressed. Various chemotherapeutic agents, steroids, and whole-body irradiation were all equally ineffective in changing the pattern of tumor development. Attempts to grow Yaba virus in various tissue cultures have not been successful.

See also abstract nos.: 143, 145, 163, 170

MISCELLANEOUS

63-269 THE PROBLEM OF MULTICENTRIC ORIGIN IN MALIGNANT MELANOMA. (Ger.) Klostermann, H. F. (Derm. Clin., U. Göttingen, Germany). Arch. Clin. Exp. Derm. 215(4):379-388, 1962.

In this review and discussion, the author considers the hypothesis of malignant melanoma as a systemic disease, the possibility of hormonal induction, surgical induction, and malignant change of benign melanomas and nevi. He concludes that none of the hypotheses advanced can be accepted as conclusively demonstrated. The problem of primary multiple melanoma is particularly thorny because of the difficulty of distinguishing primary tumor and metastasis, and in the case of induction from nevi, it remains to be determined whether the junctional activity responsible for their development may not be biologically malignant from the outset. (31 references)

63-270 A NEW APPROACH TO THE MELANOMA PROBLEM. (Ger.) Hess, P. (Bethesda Hosp., Duisburg, Germany) and D. Hess. Strahlentherapie 19(4):486-497, 1962.

Schreus's view that melanomas do not derive from epithelial cells, but from the melanocytic transformation of deep-lying Schwann cells migrating to the surface, is discussed. Personal experience with 81 cases treated with irradiation alone and 10 undergoing combined therapy is then reported. While true melanomas occurred in pts. aged 16-89 yr., the majority appeared in the fourth to seventh decades; female to male ratio was 64:47. Most melanomas appeared on the most exposed sites--face, torso, and lower extremities. In contrast to other published data, in 98 pts., melanomas had derived from pigmented nevi, 7 pts. exhibited melanomatosis blastomatosa, and in 6 pts. the melanomas were spontaneous.

63-271 FAMILIAL MULTIPLE POLYPOSIS: A GENEOLOGIC STUDY OF ONE FAMILY. (Sp.) Lopez, E. A. (Cent. Hosp. Caja, San José, Costa Rica). J. Int. Coll. Surg. 39(2):182-187, 1963.

An interesting family history of multiple polyposis was traced through 4 generations, beginning with a common great-great-grandfather, who died with cachexia, anal tumors and bloody diarrhea (possibly with adenocarcinoma of the rectum). Of the 45 members of the 4 generations, 12 (26.7%) had multiple polyposis, and 7 of these are known to have died with adenocarcinoma. Of the 4 members of the first generation, 2 died of adenocarcinoma of the rectum. In the second generation, 5/13 had the familial disease, 4 of these had adenocarcinoma. Polyposis was also found in 1/17 of the third and 3/10 of the fourth generations. Of the 12 recorded cases, 9 were males and 3 females. The 3-fourth generation pts. subjected to colectomy and permanent ileostomy

have remained well for 6, 5 and 1½ yr.

63-272 CASE REPORT OF A LEUKEMIC PATIENT WITH A DOUBLE POPULATION OF RED CELLS DIFFERING IN THEIR ANTIGENS OF THE ABO GROUP AND THE MN SYSTEM. (It.) D'Angelo, A. (Inst. Spec. Path., U. Messina, Italy) and I. Chiovato. Riv. Pat. Clin. 17(10):766-770, 1962.

Brief case report of a 28-year-old woman with acute paramyeloblastic leukemia in whom a detailed hematological examination revealed 2 types of erythrocytes: approximately 75% A₁, CcDEe, M and 25% O, CcDEe, MN. The authors emphasize that the pt. had not been given X-ray therapy and was not a twin. It is stated that this anomaly could be a somatic mutation, due to heredity or could have been incurred during the course of the disease.

63-273 ANTIGENIC PROPERTIES OF OTHER EXPERIMENTAL TUMORS. (E.) Klein, G. (Inst. Tumor Biol., Karolinska Inst., Med. Sch., Stockholm, Sweden) and E. Klein. Pp. 463-470 in Basic Mechanisms in Animal Virus Biology. V. 27 in the Cold Spring Harbor Symposia on Quantitative Biology. Frisch, L. (Ed.). Biol. Lab., Long Island Biol. Assn., 1962.

The maximum resistance to 2-methylcholanthrene (20-Me)-induced sarcomas, indicated as the minimal number of tumor cells needed to produce takes in mice pretreated with heavily irradiated tumor cells, was, for autochthonous and isologous hosts resp.: no resistance (10^4 cells grew out), 4 and --; resistance dose (R) $> 10^4$, 1 and --; R $< 10^5$, 3 and 5; R $> 10^5$, 1 and 1; R $< 10^6$, 8 and 12; R $> 10^6$, 2 and 10; R $< 10^7$, -- and 2; R $> 10^7$, 0 and 2. Minimum cell dose required for growth of 20-Me-induced sarcomas in untreated isologous hosts was higher than those for spontaneous mammary carcinoma, for implanted cellophane-induced sarcomas (see CRA 1(1):#37, 1963), or for lymphomas. Pre-irradiation with 350-400 r (whole body) diminished host resistance: 10^3 MALA tumor cells, which showed almost no growth in untreated isologous hosts had grown to 6 mm tumors in 30 days after inoculation into pre-irradiated mice. Similar breakdowns of resistance followed pretreatment with irradiated cells of other tumors, or with irradiated isologous spleen and liver suspensions. Growth of sarcomas MC 57G and MC57F in C57Bl mice was not inhibited in hosts with no pretreatment or with 400 r whole-body irradiation 24 hr. previously; but on pretreatment with 7 inoculations of irradiated spleen and liver, growth of both tumors was suppressed; after 6 inoculations of cells of irradiated MC57G sarcoma, growth was completely suppressed in the G strain and retarded in the F strain. In combined in vitro-in vivo admixture-experiments, utilizing irradiated recipient mice, a typical experiment showed that lymph node cells of isologous hosts, pretreated with and resistant to MC57R sarcoma, neutralized cells of the same tumor, but not those

of another C57B1 sarcoma induced by the same dose of 20-methylcholanthrene in another C57B1 mouse. Histologically similar cellophane film-induced sarcomas showed a comparatively weak resistance in isologous hosts pretreated with irradiated cells of the same tumor: tumors were induced by 10^3 cells in 2/19, by $< 10^4$ cells in 11/19, and by $< 10^5$ cells in 6/19 isologous hosts; autochthonous hosts showed no resistance. Since polyoma-induced tumor cells in mice appear to have a common specific antigenicity, as do also the Gross virus-induced lymphomas (or at least an extensive antigenic overlapping), it was suggested as a working hypothesis that virus tumors may have new cellular antigens for each virus-cell-host-system, analogous to the conversion phenomena in bacteria. In tumors induced by aromatic hydrocarbons, on the contrary, being characterized by highly specific antigens (as shown by the resistance that can be developed in hosts by pretreatment, and its loss after whole-body irradiation), a factor in their induction may be their concomitant reduced immunity.

- 63-274 ATTEMPT TO DIFFERENTIATE "PRECANCER" FROM "CARCINOMA IN SITU". (E.) Golbert, A. V. (Pathomorphol. Dept., Herzen's State Oncol. Inst., Moscow, USSR). Pp. 479-482 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

The author briefly reviews the literature on the development of carcinoma of the breast, stomach and uterine cervix, and agrees with those authors who distinguish 4 stages of epithelial hyperactivity: metaplasia; solitary anaplastic cells distinguishable throughout the entire epithelium; basal cell hyperactivity (the stage of precancer); and carcinoma in situ. In the last stage, the anaplastic epithelium is not yet invasive but already occupies the entire thickness of the epithelium, while precancer consists of multiple microscopic foci of proliferated epithelium. The beginning of penetration into the subepithelial stroma is very difficult to diagnose. Distinction between precancer and carcinoma in situ is important since the latter requires surgery while the former only demands repeated observation. (18 references)

- 63-275 EPITHELIAL HYPERPLASIA AND CELLULAR INFILTRATION OF THE CERVIX UTERI. (E.) Munck, W. (U. Inst. Path., Aarhus, Denmark). Pp. 483-488 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In the attempt to distinguish more precisely between the cellular changes due to cervical erosion and those due to invasive carcinoma, the author reviews the diagnostic criteria for carcinoma in situ and pays particular attention to the changes occurring in the adjacent stroma. On the basis of his own previously published work on the role of the macrophages in the growth of

transplantable tumors in mice and rats, tar-induced carcinoma and spontaneous mouse tumors, the author suggests that these cells, whose main function is the uptake of cellular waste products, may also take up growth-stimulating substances from necrotic tumor cells. This is confirmed by evidence that prolonged local irritation, resulting in epithelial proliferation and dilatation, congestion and primary anoxia of the stromal vessels, is accompanied by an increase in the number and activity of the macrophages.

- 63-276 SOME EXPERIMENTAL ASPECTS ON PRECURSORS OF GASTRIC CANCER. (E.) Torgersen, O. (Inst. Morbid Anat., State Hosp., Oslo, Norway), B. Øystese and S. Refsum. Pp. 553-564 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Extensively reviewed is the literature on the etiology of gastric cancer. In a discussion of some of the basic concepts relating to absorption of possible carcinogens from the food and blood, special emphasis is given to the effects of the mucosal barrier, gastric retention and the presence of ulceration. Following intragastric administration of iron-dextran (Imferon) to mice, the normal gastric epithelium proved to be quite resistant to the penetration and deposition of this type of carcinogen, even in the presence of pyloric obstruction. Ulcerating or regenerating mucosa may become the site of selective deposition of the agent after either p.o. or i.v. administration. Large amounts of iron, both bivalent and trivalent, were found in the connective tissue of the ulcerated area and in the proliferating epithelium when ulceration was combined with gastric retention, even in dead animals. After regeneration and differentiation, however, the mucosa returns to its usual resistant state. The authors conclude that gastric lesions per se are not the precursors of gastric cancer but may provide a locus of lower resistance to the penetration of carcinogens in the blood or gastric contents. (58 references)

- 63-277 VARIATIONS IN IRON DEPOSITION IN MAMMARY EPITHELIUM ASSOCIATED WITH CANCER SUSCEPTIBILITY AND DEVELOPMENT. (E.) Rawlinson, H. E. (Dept. Anat., U. Alberta, Edmonton, Canada). Pp. 341-347 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

When intact, female hybrid mice (Strong A x C3H), 8-10 wk. old, were implanted s.c. with 2-3 additional pituitaries from similar female and male mice, cancer incidence was 28/47 (60%) and 48/62 (77%), resp.; incidence in untreated females was 7/62 (11%). In treated females there was generally an increase in iron content of the mammary glands. The glands from either sex were equally potent. Implanted males showed a similar, but less marked effect. These results support the contention that specific mammogenic hormones are produced by the

pituitary and that this activity is more continuous in an ectopically placed pituitary.

- 3-278 BENIGN HYDATIDIFORM MOLE FOLLOWED BY LATE PULMONARY CHORIOCARCINOMA. (E.)
 Gunnar, J. (Glasgow Victoria Infirm., Scotland).
 and R. A. Tennent. J. Obstet. Gynaec. Brit. Comm. 69(6):999-1005, 1962.

A woman of 40, hysterectomized 2 yr. previously for an apparently benign hydatidiform mole, developed metastatic trophoblastic disease (pulmonary choriocarcinoma), with multiple pulmonary lesions and increased urinary gonadotropins. It was postulated that malignant transformation could have occurred after a latent period, in benign pulmonary emboli from the original benign mole. Thus hysterectomy, in cases of benign hydatidiform mole, may not eliminate the risk of malignant trophoblastic disease.

- 3-279 CONSIDERATIONS ON THE HISTOLOGICAL TYPE OF LUNG CANCER IN RELATION TO SEX. (E.)
 Di Paola, M. (Inst. Gen. Clin. Surg., U. Rome) and V. Stipa. Riv. Tuberc. 10(3):254-259, 1962.

Among 988 men and 66 women with lung cancer, 2.4% of the women and only 11.5% of the men had adenocarcinoma, which is considered to be endogenous; 87.1% of the men and 48.5% of the women "exogenous" undifferentiated or Malpighian carcinomas. This is considered to be further statistical evidence for the importance of smoking in the etiology of lung cancer, since air pollution affects both sexes equally. Additional confirmation was provided by the fact that, in women, adenocarcinoma was discovered in only 1/6 who smoked > 20 cigarettes/day, compared to 2/3 who smoked less. The authors suggest that the incidence of the exogenous forms of lung cancer in women will probably increase in the future, due to the increasing prevalence of smoking.

- 3-280 CANCER AND THE ORTHODOX JEW. (E.)
 Zadik, P. (Haifa, Israel). Hebrew Med. 2:249-244, 1962.

In a general review of some of the biblical commands which may have a prophylactic effect against cancer of various organs, the author discusses the incidence of cancer of the breast, penis, cervix, skin, lung and bladder among orthodox and non-orthodox Jews and suggests reasons for some of the observed differences. Some of the interrelationships discussed are the prophylactic effect of frequent pregnancies against mammary carcinoma, the effect of circumcision on cancer of the genitalia, the role of solar radiation in skin cancer, the effect of smoking, and the possible beneficial effects of fasting and general moderation.

- 63-281 EXPERIMENTAL STUDIES ON GROWTH-PROMOTING AND GROWTH-INHIBITING SUBSTANCES OF MALIGNANT TUMOR. I. GROWTH-PROMOTING AND GROWTH-INHIBITING SUBSTANCES EXTRACTED FROM SUBCUTANEOUSLY TRANSPLANTED EHRlich ASCITES TUMOR IN MICE. (E.)
 Sugihara, Y. (Dept. Path., Hiroshima U. Sch. Med.) and F. Araki. Gann 54(1):1-10, 1963.

Saline extracts of s.c. transplanted mouse Ehrlich ascites tumors, and tumors of mice previously treated with X-ray, were separated into 6 fractions: a 30%-ethanol precipitate, the supernatant from 70% ethanol, and 4 ammonium sulfate fractions of the precipitate at 30-70% ethanol (0-30%, 30-50%, 50-70% ammonium sulfate precipitates and the supernatant after 70% saturation). Aqueous solutions of the 12 fractions (12-14 injections in 23-27 days, i.p.), were employed to treat Ehrlich ascites tumors transplanted s.c. in ddN mice 9 days before. Most of the fractions had no significant effect on tumor growth or survival time. However, the 0-30% ammonium sulfate fraction of non-irradiated tumors and the 50-70% ammonium sulfate fraction of X-irradiated tumors showed inhibitory activity, and the 70% ammonium sulfate supernatant of X-irradiated tumors seemed to promote tumor growth. The 30% ethanol precipitate of non-irradiated (but not of X-irradiated) tumors seemed to contain a toxic factor. The various fractions did not differ in their microscopic effects.

- 63-282 CHANGES IN THE AGE COMPOSITION AND MORTALITY DUE TO CANCER IN THE POPULATION OF VIENNA. (Ger.) Horak, W. (Munic. Office Stat., Vienna). Krebsarzt 17(11-12):485-490, 1962.

In a statistical study based on the census of March, 1961, the author calculates the age-specific mortality due to cancer of various organs and compares these figures with those for 1951 and earlier years. In a Viennese population which continues to age, the over-all mortality due to cancer increased by 13% for both women and men during the past 10 yr. (305 and 378, resp., per 100,000). However, all of this increase for women and 10% of it for men could be ascribed to the increase in age of the population and 3% with the increase of cancer mortality in men over 65-years of age. There were significant decreases in cancer mortality for men between the ages of 40-50 and for women aged 30-40, while that for men over 65 increased by 11%. The most common localizations continued to be the gastrointestinal and respiratory tract for men and the gastrointestinal tract, genital tract and breasts for women. In a period of 10 yr. (1951-61) cancer of the respiratory tract in men increased from 106 to 128; of the urinary tract, from 13 to 28; in women, cancer of the mammary gland increased from 34 to 43; of the respiratory tract from 13 to 18; of the liver, bile and pancreas from 37 to 43; of the urinary tract from 6 to 14. In the same period of time, there were significant increases (recalculated per 100,000) in age-specific mortality due to cancer of the respiratory tract (age 65 or more: in men,

from 426 to 579; in women, from 44 to 62), breast (age 60-65: in women, from 51 to 81), and urinary tract (age 50-60: in men, from 15 to 32; age 60-65: in men, from 27 to 58; in women, from 7 to 37; age 65 or more: in men 80 to 137; in women 27 to 45). There were significant decreases in age-specific mortality due to cancer of the respiratory tract in men between 40 and 50 yr. of age (from 39 to 12), buccopharyngeal cavity in men between 60 and 65 (from 29 to 9), esophagus and stomach in men between 60 and 65 (from 179 to 121), and the genital tract in women between 30 and 40 (from 21 to 11).

- 63-283 LUNG CARCINOMA IN WOMEN. (Ger.) Steinmann, E. P. *Zschr. Laryng. Rhinol. Otol.* 41(12):870-876, 1962.

Thirty cases of female pulmonary carcinoma were discussed and compared with others reported in the literature as to: sex and age distribution, histology and clinical findings. Statistically, women appeared to be no more susceptible to lung cancer than in the past; and incidence of epidermoid, adeno-, and undifferentiated carcinomas was about equal (33.3, 30, and 36.7%, resp.). Incidence of lung cancer was highest early in the 7th decade while highest incidence of uterine cancer occurred usually 10-15 yr. earlier. Effects of exogenous carcinogens could not be determined. Distribution of the three types of lesions in the bronchial tree resembled that for males: adenocarcinomas usually in the lower lobe and periphery, undifferentiated carcinoma attacked primarily the main bronchi and upper lobe.

- 63-284 EXPERIMENTAL INVESTIGATIONS ON METASTASIS. (Ger.) Döntenwill, W. (Inst. Path. Ludwig-Maximilians-U., Munich, Germany), U. Mohr and P. Heuck. *Klin. Wschr.* 41(2):86-87, 1963.

Yoshida sarcomas were implanted s.c. into 3 groups of Sprague-Dawley rats. From Group I the cherry-sized tumors were surgically excised 5-8 days after implantation; in Group II, the tumors were tied off with elastic bands (these necrotized and were sloughed off in 2-3 days); Group III received tumor homogenate (0.5 ml/wk. x 4, s.c.), the last dose was given 10 days prior to tumor implantation. Incidence of metastases was: controls, 19/37 (51.4%); Group I, 15/23 (65.2%); Group II, 21/26 (80.6%); Group III, 11/14 (78.6%). Metastases were predominantly in the mesenteries and intestinal lymph nodes (58.7%) and in the thymus and bronchial lymph nodes (19.3%). Survival times were: controls, 20.8 days; Group I, 26.5 days; Group II, 28.2 days; and Group III, 20.7 days. Similar results were obtained in experiments on golden hamsters with transplantable plasmacytoma KG 13. The increase in metastasis formation is chiefly related to conditions of better nutrition which follow removal of a primary tumor, rather than to mechanical factors connected with tumor excision.

- 63-285 MORPHOLOGICAL PRECURSORS OF CANCER: THEIR SIGNIFICANCE IN CANCER CONTROL. (E.) Heller, J. R. (Sloan-Kettering Inst., New York). Pp. 45-51 in *The Morphological Precursors of Cancer*. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In a discussion of what constitutes a precancerous tissue change, the problem of *in situ* preinvasive cancer is considered, its progress, growth patterns, reversibility and epidemiology. In a 10 yr. follow-up study of more than 150 pts. with cervical lesions and of 110 with cervical carcinoma *in situ*, 2 untreated pts. of the *in situ* group progressed from atypical lesions to definite carcinoma. The potential malignancy of rectal polyps is also discussed. Between 1946-1954, a total of 26,126 asymptomatic men and women underwent 47,091 proctosigmoidoscopic examinations: carcinoma was diagnosed in 58 pts. (0.22%); *in situ* lesions were identified in 47 (0.18%). In 4 asymptomatic individuals carcinoma was found at sites where adenoma had previously been diagnosed but resection had been refused; in one instance the interval had been 13 yr. The author believes that a significant number of so-called benign adenomas progress to carcinoma. Some factors mentioned as contributing to the transformation of a normal to a malignant cell are: endocrine imbalance; virus; physiological misuse of vitamins; and metabolic variations (especially in enzyme activities). Host resistance and immune mechanisms are briefly considered.

- 63-286 DOWN'S SYNDROME (MONGOLISM), OTHER CONGENITAL MALFORMATIONS AND CANCERS AMONG THE SIBS OF LEUKEMIC CHILDREN. (E.) Miller, R. W. (NCI, Bethesda). *New Eng. J. Med.* 268(8):393-401, 1963.

Among 459 white American children whose leukemia was diagnosed between 1958 and 1961, 6 had Down's syndrome, 22 had other major, and 36 minor, congenital defects. In 6 families, more than 1 child was affected. Among 1000 sibs of the index children, 4 had Down's syndrome; 26 (2.6%) had other major congenital defects (matched controls, 2.5%); 8 had cancer (including 5 cases of leukemia), expected incidence 1; 30 died of causes other than cancer; among the mothers there was some pregnancy wastage. The high incidence of Down's syndrome in both the index children and their sibs, compared to matched controls, was highly significant. Chromosomal defects (translocations or primary nondisjunction) are commonly associated with mongolism, and various chromosomal aberrations have been reported in leukemics. However, the association of leukemia with chromosomal abnormalities does not necessarily imply a cause and effect relationship. It may indicate only that chromosomal defect predisposes to vulnerability to an environmental carcinogenic agent.

- 63-287 AN UNCOMMON BLOOD GROUP ISOANTIBODY (ANTI-M) IN NEOPLASTIC DISEASE. (E.) Klein, S. J. (VA Hosp., Long Beach, Calif.),

E. B. Reilly and J. J. Matsushima. Nature (Lond.) 197:393-394, 1963.

Of 10 pts. found to have anti-M antibodies in their plasma (all with NN blood), 9 had neoplastic disease (6 carcinomas, 3 uterine leiomyomas); 1 had a bleeding duodenal ulcer. Two of these were among 15 M-negative cancer pts. found among 173 tested. Cancer tissue obtained at surgery showed in one pt. an almost complete absorption of anti-M, and some absorption in that of the second, but little or no absorption by non-cancerous segments of the same tissue pieces. It might be desirable to look for neoplasm in pts. who present anti-M, especially in the absence of known M-antigen stimulus.

63-288 HISTOLOGICAL CHANGES IN THE BRONCHIAL EPITHELIUM AS A POSSIBLE PRECANCEROUS STATE AND THEIR RELATION TO THE CYTODIAGNOSIS OF BRONCHIAL CANCER. (E.) Svejda, J. (Dept. Path., Fac. Med., U. Brno, Czech.). Pp. 643-654 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

The rising frequency of bronchial cancer increases the urgent need for improved early diagnosis (frequency 1950 and 1960: men, 45 and 110; women, 5 and 20). In a study based mainly on older men with bronchiectasis and bronchitis, significant early changes in the bronchial epithelium were squamous metaplasia with proliferation of atypical cells, and basal cell proliferation, with squamous cells in the outer layer. Such changes would indicate the need for frequent reexamination. Squamous metaplasia with regular bronchial epithelium, well delimited from the lamina propria and without increased proliferation; or, hyperplasia of basal cells without penetration into the lamina propria, are less apt to lead to malignancy. In some cases of bronchial carcinoma, precancerous epithelial changes were found in widely separated areas, suggesting a multicentric origin.

63-289 ABOUT PRECANCEROUS LESIONS IN HUMAN BREAST. (E.) Vogt-Hoerner, G. (Gustave-Roussy Inst., Villejuif, Seine, France) and D. Aryen. Pp. 411-416 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Of 151 pts. treated for sclero-cystic and proliferating mammary dysplasia, 73 were lost to follow-up; none of 18 treated by simple mastectomy as a precautionary measure and followed for 5-10 yr. developed carcinoma. Among 60 other pts. followed 1-15 yr., none developed carcinoma. The difficulty is emphasized of detecting, microscopically or submicroscopically, the moment of cell transformation to malignancy. In the dysplastic tissue in the immediate vicinity of two early cancers, functional disturbances of the epithelium were found: there were PAS-positive granulations in the cytoplasm of tubulous or

acinous epithelium, where they were widely but irregularly distributed in basal, apical, and paranuclear regions. In other cases, dysplastic tissue was found near (but not in) well developed cancer, but never in proliferating mastitis that remained benign. The authors do not claim to have found a precancerous occurrence, but they suggest its possible usefulness to encourage more intensive study in the diagnosis of a doubtful lesion.

63-290 A RECONSIDERATION OF SCAR CARCINOMA OF THE LUNG. (E.) Tonelli, L. (Inst. Surg. Path., U. Perugia, Italy). Pp. 621-624 in The Morphological Precursors of Cancer. Severi, L. (E.). Perugia, Div. Cancer Res., 1962.

Based on a study of more than 300 fresh surgical specimens of round peripheral lung carcinomas, where a scar was present in about 40%, the author disagrees with the Rössle interpretation of such forms as "scar carcinoma or Narbenkrebs", which develop in old pleuropulmonary scars, their growth enhanced, perhaps by deposits of cholesterol which structurally resembles chemical carcinogens. The so-called scars are pleural depressions, not pre-existent to the tumor but caused by the tumor. He considers the pleural depression is a consequence of the traction exerted by the interlobular septa which in turn is caused by the tumor growing in the lumen of a peripheral bronchus and distending it enormously. They almost certainly do not correspond to previous infarcts, are not tubercular, and occur mostly in pts. 40-50 yrs. old. These depressions are peculiar to lung tumors, and as such have diagnostic value for the surgeon at exploratory thoracotomy. In a subsequent discussion, Baló showed slides of typical hemorrhagic infarcts of the lung, and stated that he had observed that from the scars of the infarcts peripheral carcinoma can arise.

63-291 THE QUESTION OF NUCLEAR STABILITY DURING HISTOGENESIS, AGING, AND CARCINOGENESIS. (E.) Walker, B. E. (Dept. Anat., U. Texas Med. Branch, Galveston). Cancer Res. 23(2) (Pt.1): 157-164, 1963.

In the hope of bringing together some of the newer concepts concerning the basis for progressive and regressive changes during an organism's life cycle, and exploring the possibilities of interrelating them in a single biological theory of individual development, with special reference to the genetic apparatus of the cell, the author reviews the literature (82 references) on the role of nuclear and of cytoplasmic heredity in the processes of ontogenesis, organogenesis, carcinogenesis and aging. Particular attention is given to alterations in chromosome number and to the role of somatic mutations in general in the mechanisms of normal differentiation and aging. The consequences of the contrasting hypothesis of nuclear stability and instability are compared at various levels of biological complexity. Carcinogenesis is then discussed from the points of view of changes in mitosis

and the carcinogenic viruses, and aging is discussed in terms of inadequate cell behavior. The basis for understanding these varied phenomena is the concept of random mutations occurring with a significant frequency in somatic cells but normally kept under control by homeostatic factors within the organism. Carcinogenesis and aging would then occur when the period of the life cycle under positive influence by natural selection had passed, or when novel or sporadic agents adversely affected the stability of the nucleus.

- 63-292 KERATOACANTHOMA. (E.) Rook, A.
(United Cambridge Hosp., England) and
R. H. Champion. Nat. Cancer Inst. Monogr. (10):
257-273, 1963.

The incidence, etiology, and clinical and histological characteristics of keratoacanthoma are discussed on the basis of statistical data from 222 personal cases and an extensive review of the literature (47 references). The geographical and racial distribution of keratoacanthoma appears to parallel that of squamous carcinoma. Keratoacanthoma is 3 times as common in males as in females, with a fairly constant incidence after the age of 55. Sunlight and exposure to carcinogens are implicated in the etiology, and most lesions occur on the exposed skin. Despite frequent association with recent trauma, the presence of a virus has not been conclusively demonstrated. Keratoacanthoma is a benign tumor which is usually derived from the outer root sheath of the upper part of the hair follicle and the contiguous surface epithelium, or occasionally from the lower part of the follicle. After an initial period of rapid growth, the lesions are generally static and show a marked tendency to regress spontaneously, even when the histological features are indistinguishable from those of squamous carcinoma. In the experimental animal, continued application of carcinogens leads eventually to malignant transformation; an analogous situation may arise as the result of slowly progressing degenerative changes in man.

- 63-293 SKIN CANCER IN INDIA. (E.) Mulay,
D. M. (Willingdon Hosp., New Delhi,
India). Nat. Cancer Inst. Monogr. (10):215-223,
1963.

Following a brief description of the climate of India and the racial composition and social pattern of its population, the author describes the clinical features, course and incidence of the various types of skin cancer found and suggests several hypotheses as to their etiology. In general, the incidence of skin cancer is quite low among Indians, being 1.4% of all carcinomas compared to 18.4% in resident Europeans. Data are given on the distribution of basal cell carcinomas in Indians and Europeans by site and histological type. Squamous-cell carcinoma on the trunk is relatively common in Indians, and is attributed to the effects of chronic irritation

due to the wearing of a dhoti (loincloth). Other specifically Indian cancers are carcinoma of the hard palate due to chutta smoking, with the burning end of the cigar inside the mouth; khaini cancer of the lip due to the use of a mixture of tobacco and lime which is placed in the groove between the lip and the front teeth; and oral cancers due to betel leaf or accra nut chewing (sometimes combined with tobacco). Penile cancer is practically unknown in Mohammedans, who practice circumcision. In 3 series of cases, 25%-53% of cases of malignant melanoma occurred on the foot, which would indicate that trauma can be an exciting factor, since most of the pts. walked barefooted.

- 63-294 VARIATIONS IN SKIN CANCER INCIDENCE
WITHIN THE UNITED STATES. (E.) Haenszel,
W. (NIC, Bethesda). Nat. Cancer Inst. Monogr.
(10):225-243, 1963.

Previously published data from the 10-city and Iowa morbidity surveys of 1947 and 1950 were retabulated and supplemented by new data from the New York Cancer Register (upstate) for 1958-60. The fact that the slopes of curves of age-specific rates are as much a function of site as of histological type, and the fact that the increased risk of skin cancer in rural southern males is more pronounced for the face, head, neck and upper extremities than for the trunk and lower extremities, seem to confirm the role of sunlight as a skin carcinogen. Incidence of all skin cancers (per 100,000) for males and females, in 4 northern cities is 33.4 and 25.4; for 4 southern cities, 143.3 and 88.0, resp. This North/South gradient holds for basal and squamous cell carcinomas, as well as for melanomas. Although the face, head and neck showed the highest incidence per unit area, the upper extremity lesions were more indicative of variability in risk, with very high male/female and North/South ratios for both of the types of carcinoma; the importance of upper extremity lesions was also shown by the fact that the basal-cell age curve was much flatter than that for squamous carcinoma, while in other sites the slopes were approximately equal. Incidence of melanoma in females was higher than in males. The author concludes that more detailed analysis of data may help in answering some of the etiological questions, but that true advances in epidemiology will depend on improvement in the quality of the data collected.

- 63-295 TESTICULAR ATROPHY FOLLOWING MUMPS. A
CAUSE OF TESTIS TUMOUR? (E.) Kaufman,
J. J. (Dept. Surg. Urol., U. Calif. Med. Ctr., Los
Angeles) and P. T. Bruce. Brit. J. Urol. 35(1):
67-69, 1963.

A pt., age 30, developed orchitis with subsequent testicular atrophy 1½ yr. after infection with mumps. A seminoma in the affected testicle was managed by radical orchiectomy; an abdominal enlarged lymph node was also removed. Microscopic sections showed that the seminoma had developed

in juxtaposition to atrophic tubules. On the basis of these findings, and in view of reports by others of the higher incidence of testis tumors in the cryptorchid or atrophic testis, and in line with experiments of others with metal-induced (zinc chloride) testis tumors in roosters, it is concluded that atrophy per se, of whatever origin, may be causally related to testicular oncogenesis.

63-296 SOME STUDIES ON EXPERIMENTAL TUMORIGENESIS: TUMORS IN TRANSPLANTED PITUITARY GLANDS. (E.) Gardner, W. U. (Dept. Anat., Yale U. Sch. Med., New Haven, Conn.). Pp. 89-106 in On Cancer and Hormones: Essays in Experimental Biology. Chicago, U. Chicago Press, 1962. \$8.50.

One to 4 pituitary glands (both anterior and posterior lobes), were transplanted s.c. into females of the same strain of mouse (C57, CBA, and BC) or hybrid groups (C3H x BC and C57 x BC, designated CB and PC, resp.); subsequently, tumors appeared only in mice that survived 500 days or more. In BC and C57 hosts there were 44/64 and 5/19 successful grafts; 14 and 2, resp., became tumorous. In CB and PC hosts there were 6/6 and 8/11 successful grafts; 6 and 4, resp., became tumorous. All tumors were small, fleshy or fibrous masses, encapsulated by connective tissue, and well vascularized. The success of transplantation was not influenced by the number of glands implanted, nor by the age of donor or host. In mice bearing extra pituitary transplants, the number and duration of periods of estrus-type vaginal exfoliates decreased with increasing number of pituitary grafts per host, and the number of days between cycles increased. All pituitary tumors were small-celled, chromophobic, some compact, some sinusoidal, resembling the tumors of estrogen-treated mice. Genetic influence was expressed only in strain differences in tumor formation. In the CBA line, no pituitary tumors appeared, but all had mammary cancer. Pituitary tumors occurred in estrogen-treated BC mice, especially when given in small doses over long periods. Mice of the CB group were very susceptible to tumors. The tendency for pituitary grafts to become tumorous may be strain-limited, and may parallel the tendency to become tumorous after exposure to estrogen. The possible endocrine interrelations involved are considered.

63-297 DEMOGRAPHIC AND EPIDEMIOLOGICAL CONSIDERATIONS ON CANCER. (Sp.) Olascoaga, M. L. Rev. Sanid. Milit. Argent. 61(2):126-134, 1962.

After pointing out some of the reasons for the apparent worldwide increase in cancer mortality (longer life span, better diagnosis and reporting), the author discusses the incidence of cancer in Argentina and particularly in Mendoza, showing that cancer accounts for 13%-14% of all deaths, with the digestive tract the most common localization in both sexes (stomach for men and liver

for women). Finally, he reviews some of the recent work on the role of the environment in the etiology of cancer, dividing environmental cancer into malignancies produced by the prolonged effect of irritative agents such as As, sunlight or schistosomiasis, those produced by habits such as smoking and tobacco chewing, and occupational cancers due to As, Cr, Ra, aromatic dyes and other agents; he points out that the organs most commonly affected by environmental cancer are the skin, lips, tongue, mouth, lungs, liver, kidneys, bladder and connective tissue. After pointing out the value of a comparative study of the incidence of environmental cancer in man and animals in relation to the local conditions, the author described the study carried out by R. Cameron in Hagerstown, Iowa in 1958 in some detail.

63-298 HEREDITARY ADENOMATOSIS OF THE COLON AND RECTUM. (Sw.) Alm, T. (St. Eriks Hosp., Stockholm, Sweden), B. Lindholmer and A. Reuterskiöld. Nord. Med. 69(1):33-37, 1963.

A preliminary study confirmed the presence of colorectal adenomatosis in 2 or more successive generations of 17/21 families investigated; or a total of 115/288 related individuals (40% of the study population). The presence of cancer was confirmed in 62 (21%). Simultaneous colorectal adenomatosis and colorectal cancer occurred in 38/62. In 17/62, who also had colorectal cancer, adenomatosis was probable, but could not be established conclusively; 7 cancer deaths had occurred in the absence of sufficient information to make localization certain. Cancers outside the colorectal tract were also found in 4 additional subjects. The mean age at death for cancer cases was 46 yr. The authors conclude that colorectal adenomatosis can be transmitted as a Mendelian dominant with a very high risk of eventual carcinogenicity and malignant degeneration, which usually sets in before the age of 40. Since the disease is usually asymptomatic prior to the approach of malignant transformations, they feel that surgery should be performed as soon as diagnosis is made; and suggest that all members of families in which the condition has occurred should be examined every 2-3 yrs., beginning at age 12-13.

63-299 TECHNIQUES AND METHODS IN STATISTICS AND EPIDEMIOLOGY OF SKIN CANCER. (E.) Higginson, J. (Dept. Path., U. Kansas Med. Ctr., Kansas City). Nat. Cancer Inst. Monogr. (10): 649-652, 1963.

The author reviews some of the additional precautions made necessary in the evaluation of comparative studies in skin cancer by the high rate of cure of many skin tumors and by the difficulty in assessing the malignancy of some. He points out that relative ratio studies reporting the number of skin cancers as a proportion of all cancers or of pts. admitted can only be used, with care, to compare distribution by site and histological pattern. Mortality rates are of no value

because of the high rate of cure of skin cancers. Morbidity data from different geographical areas should always include data permitting comparison by site and histological type. Studies of pre-cancerous lesions and etiological factors should include data on the proportion of rural and urban pts., nature of occupation, exposure to known or possible carcinogens (including sunlight) and the prevalence of albinism.

- 63-300 SKIN CANCER IN AFRICA. (E.) Oettle, A. G. (S. African Inst. Med. Res., Johannesburg). Nat. Cancer Inst. Monogr. (10): 197-214, 1963.

In a broad review of all the available epidemiological information on skin cancer in the African, the author presents morbidity data only for the Johannesburg Bantu, followed by mortality rates for the "white", "colored" and "Asian" populations of South Africa, ratios of skin cancers in histological series in Negroids in various parts of Africa, and a large amount of data from the Transvaal histological survey (1949-53) regarding skin cancer in whites, in pigmented Bantu and in albino Bantu, the frequency of nevi in pigmented Bantu, the frequency of albinism in South African Bantu, the occurrence of skin cancer in Bantus with xeroderma pigmentosum, and the absence of skin cancer in vitiliginous skin. The data available indicate a low incidence of skin cancer in the pigmented races, particularly basal-cell and squamous-cell carcinoma and melanoma, while adnexal tumors are equally frequent in all races. Although the high rates observed in the exposed skin of whites and the albino Bantu are mainly attributable to sunlight, additional etiological factors must be involved in the pigmented races, especially for lesions of the lower extremities; these factors include chronic ulceration, trauma (particularly that due to burns), uncleanness, and the use of tobacco.

- 63-301 KAPOSI'S SARCOMA IN AFRICA. (E.) Oettle, A. G. (S. African Inst. Med. Res., Johannesburg). Nat. Cancer Inst. Monogr. (10):281-285, 1963.

Incidence of Kaposi's sarcoma is exceptionally high among African Negroes (1.6-3.1/100,000), even though the incidence is low in contiguous non-Negroid populations. The incidence increases with age and is much higher in males, although this is not true for South African whites or for Algerians. The incidence varies from 20 times the USA rate in Johannesburg to 40 times the USA white rate in Uganda. In most areas, Kaposi's sarcoma accounts for 1-4% of all cancers, rising to 9.1%-12.8% in the northeastern Congo. The histopathology and anatomical distribution are the same as in Caucasians, but no cases with co-existing lymphomas or leukemia have been seen in Negroes. Since the incidence in American Negroes is the same as in Caucasians, genetic factors seem unlikely and the high incidence in Africans

is probably to be explained by still unknown environmental factors.

- 63-302 THE PRESENTATION OF MALIGNANT MELANOMA (MELANOBLASTOMA). (E.) Milton, G. W. (Dept. Surg., U. Sydney, Australia) and C. W. D. Lewis. Med. J. Aust. 1(7):239-242, 1963.

Among 91 cases of malignant melanoma recorded in Sydney and Perth during the past 3 yr. were 54 women and 37 men, average age was 48 yr.; 87 were of British or Northern European stock; skin type was fair in 39%, brunette in 43% and bronze in 15%; 52% of the pts. tanned easily, 43% burned red and 15% freckled. Only 5% had lived more than 2 yr. in the tropics; 65% had indoor occupations, but 66% engaged in outdoor sports and hobbies. Of the lesions themselves, 32 were on the leg and foot, 24 on the head and neck, 18 on the trunk and 12 on the arm and hand (thus mostly in exposed areas). In 14 cases, there was a family history of skin tumors, but only 1 pt. had a blood relative with malignant melanoma; 23% had a family history of cancer at some other site. Two pts. had worked in chemical factories, 15% had suffered repeated frictional trauma at the site of the melanoma and 12% had received an injury at the site. Nearly half did not recall any lesion at the site prior to the development of the melanoma.

- 63-303 CANCER CONTROL. FIRST REPORT OF AN EXPERT COMMITTEE. (E.) WHO Techn. Rep. Ser. 251:3-27, 1963.

This report deals with all avenues of cancer control as they apply to the community, medical and technical lay personnel, research, the pt. and the public at large. Under "Prevention", particular emphasis is placed on the elimination of carcinogens from industry, food additives and cosmetics, the role of cigarette smoking and air pollution, the dangers of radiation and the need for early treatment of precancerous lesions. The organization of cancer control must include a central planning body and increasing use of statistical data, for which a cancer registry is recommended. Some of the research areas discussed included investigations into the pathogenesis of cancer, the host-tumor relationship, and the nature of the normal and malignant cell.

- 63-304 SKIN CANCER IN SINGAPORE. (E.) Shanmugaratnam, K. (Dept. Path., U. Singapore) and E. B. La'Brooy. Nat. Cancer Inst. Monogr. (10):127-140, 1963.

Limited available morbidity and mortality data shows a low incidence of skin cancer in Singapore but a relatively high mortality from skin cancer expressed as percentage of all cancers. Chinese comprise 73% of the population, Malays 13%, East Indians 11%; 52% are under the age of 20. Between 1950 and 1961, 493 cases of superficial cancer were diagnosed and included 32 melanomas, 18 can-

cancers of the lip, vulva 20, penis 65, scrotum 6 and 352 of the skin (174 squamous-cell, 164 basal-cell and 14 adnexal carcinoma). Part of the further detailed analysis showed that the melanomas occurred mostly on the feet (in contrast to the usual head and neck localization in Caucasians) and were less common than in rural areas. Skin cancer incidence was higher among Caucasians, and was lowest among the darker East Indians; the increase in squamous-cell and decrease in basal-cell carcinomas was correlated with the depth of skin pigmentation. Racial variations in the distribution of squamous-cell carcinoma by site are discussed. Lip cancer was also more common among Caucasians and Indians. The incidence of penile carcinoma was lower than in China and India, but there was no significant difference between the incidence in circumcised Malays and that in uncircumcised Chinese and Indians.

63-305 RESOLUTIONS AND RECOMMENDATIONS OF THE CONFERENCE ON THE BIOLOGY OF CUTANEOUS CANCER. (E.) Nat. Cancer Inst. Monogr. (10): 657-660, 1963.

Among the resolutions, covering broad approaches to the study of skin cancer, were many specific recommendations in the fields of epidemiology, demography and environmental and other etiological factors. Many of the problems in the assay of potential carcinogens are outlined, and various potentially useful tests are mentioned; this subcommittee feels that other reliable predictive technics should be encouraged.

63-306 MALIGNANT TRANSFORMATION OF A RETRO-STERNAL THYROID GOITER. (It.) Fazzini, P. F. (Inst. Anat., U. Florence). Arch. De Vecchi Anat. Pat. 37(2):479-498, 1962.

Histological examination of a retrosternal tumor, the size of an orange in a 54-year-old woman revealed a follicular type of thyroid carcinoma. After a detailed review of the literature and a theoretical discussion of the problems of migration of thyroid tissue and malignant degeneration of benign thyroid goiters and on the basis of his own histological findings, the author concludes that a nodular goiter, in his pt., migrated from the thyroid to the anterior mediastinum, where it underwent malignant degeneration to thyroid carcinoma.

63-307 ON PRECANCEROUS AND PRESARCOMATOUS CHANGES IN THE THYROID GLAND. (E.) Walther, B. (Inst. Path., U. Berne, Switzerland). Pp. 745-749 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Malignant epithelial and sarcomatous thyroid growths develop almost exclusively from single or multiple adenomas. Some adenomatous nodule

tissue cannot be diagnosed with certainty as benign or malignant. Evidence of precancer is sometimes found in adenomas which are usually parenchymatous, in which medium to broad strands as well as narrow solid epithelial formations appear. Papillomas and Hürthle cell adenomas are definitely precancerous. Iodine prophylaxis in Switzerland has led to the disappearance of struma diffusa of the newborn, and to thyroid normalization up to 40 yr. Adenomas have become less frequent, but struma maligna (thyroid carcinoma) has not decreased, and young people suffer from it more frequently than before. Malignant sarcomatous strumas too are derived from adenomas. Where goiter is endemic, as in Switzerland, hemangioendothelioma and reticulosarcoma may develop, not from an adenoma, but directly from the thyroid gland itself.

63-308 STUDIES ON THE TRANSPLANTABLE DEALS GUINEA PIG TUMOUR. (E.) Haranghy, L. (2nd Dept. Path. Anat., U. Budapest, Hungary), G. Goracz, A. Kadar and Z. Kovats. Pp. 75-81 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Splenectomy or the preinjection (4 x) of 3.3 ml of homogenates of Deals transplantable guinea pig tumor failed to increase the number of tumors developing (45.5%) 7-10 days after s.c. implantation in the inguinal region of guinea pigs of both sexes. Of 56 tumors observed microscopically, 25 were macrocellular, 15 microcellular, and 9 round cell sarcomas with rapid infiltrative tendencies, while 12 were fibrosarcomas with fibroma like structures at the borders. No tumors could be induced by the injection of tumor cell free filtrates, nor did these preparations enhance the course of tumorigenesis with 3,4-benzpyrene. Chemical comparison with Guerin's tumor showed that Deals tumor contained less calcium than the former and that it also contained serine.

63-309 GASTROINTESTINAL PRECANCEROUS CONDITIONS: A STATISTICAL SURVEY. (E.) Giunti, G. (Inst. Morbid Anat., U. Bologna, Italy), A. Piccaluga and O. Narvallo. Pp. 565-572 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Among 1,119 cases of gastric disease, 442 were malignant and 562 were benign. Included among 115 (10.27%) undergoing malignant change were 17.19% of those with ulcer, 12.26% of chronic gastritis pts. and 19.23% of those with benign tumors. There was a greater incidence of malignant change in women with chronic ulcers as compared to men. Women were generally affected at a somewhat more advanced age than men. Mean age of onset (both sexes) for simple benign conditions was 51.6 yr.; for conditions undergoing malignant change, 54.1 yr.; and for primary malignancies, 57.3 yr. Typical ages of onset, for ulcers, were: benign 45-55 yr.; secondary malignant 50-60 yr.; and primary malignant 55-65 yr. Chronic ulcer thus appears to be a real precancerous disease.

Ulcer localization data showed that the pyloric antrum was a favored site. Data on 578 intestinal disease cases indicated that intestinal lesions developed at an earlier age in women than in men. Thus statistical treatment of the data in 1730 cases supports the reality of the term 'precancerous lesion' in gastrointestinal disease, this notion being previously based only on morphological grounds.

- 63-310 CIRRHOSIS AND PRIMARY CANCER OF THE LIVER. (E.) De Minjer, A. (Inst. Path., U. State, Utrecht, Holland). Pp. 199-201 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

A brief review in which it is mentioned that out of 889 autopsies in which 41 cases of cirrhosis were found, two were associated with carcinoma of the liver. The author discusses the predisposing influence that cirrhosis appears to have on the incidence of liver tumors, which are thought to be the result of regenerative activity. (9 references)

- 63-311 HEREDO-FAMILIAL DISEASE OF THE MESENCHYMAL TISSUES: CLINICAL AND LABORATORY STUDY ON ONE FAMILY. (E.) Wolf, J. K. (Variety Club Heart Hosp., Minneapolis, Minn.), M. Gokcen and R. A. Good. J. Lab. Clin. Med. 61(2):230-248, 1963.

On the basis of a genetic analysis of a family with 40 members in which acquired agammaglobulinemia and rheumatoid arthritis were associated with a high frequency of thrombopenic purpura, lupus erythematosus, rheumatoid arthritis, rheumatic fever, regional enteritis, hypergammaglobulinemia, deficiency of immunoglobulins and possible malignancies of the leukemia-lymphoma group among the close relatives, the authors speculate as to the etiological relationship between abnormalities of immunoglobulin production, mesenchymal diseases, and malignancy. While 1 case of idiopathic lymphadenopathy and 2 questionable diagnoses of leukemic reticuloendotheliosis and Hodgkin's disease among 40 pts. is not conclusive evidence of a relationship, further study would be indicated.

- 63-312 LATENT ERYTHROCYTE TURNOVER, ERYTHROPOIESIS AND CANCER. A CONTRIBUTION TO THE QUESTION OF THE ETIOLOGY OF CANCER. (Ger.) Eilers-De Cousser, T. (Nauklerstr. 18, Tübingen, Germany). Oncologia (Basel) 16(2):123-132, 1963.

On the basis of hematological and pathological studies in rats fed 4-dimethylaminoazobenzene (DAB; 5 mg/day), application of 3,4-benzpyrene or X-irradiation, the author draws a parallel between erythropoiesis and the processes responsible ultimately for tumor growth. During the treatment with DAB, Heinz-bodies were observed in 80-90% of RBC, which had a survival time of 10 days. Since the normal survival time

of rat RBC is 80 days, RBC turnover during treatment was increased about 6 times. Carcinogens generally produce erythrocyte damage which leads, in turn, to exhaustion of normal erythropoiesis and the consequent reactive formation of extra-medullary erythropoietic cells preferably in the liver, producing malformed erythrocyte precursors which have much in common with cancer cells; eventually, the reduced capacity of the mesenchymal tissue to differentiate results in the accumulation of abnormal reticulocytes and mesodermal cells; finally, embryonic erythropoietic growth appears, characterized by intravascular and later extravascular proliferation, infiltrative and destructive growth, and the formation of hemangiosarcomas. Thus, cancer growth follows the laws of embryonic erythropoiesis, but in a disordered manner. In DAB-treated rats, it is possible that the formation of cancerous cells in the liver parenchyma may be related to metabolic overload, proliferation of the bile ducts to inadequate drainage. The erythropoietic differentiation of tumor tissue is illustrated by a number of histological sections from cases of human sarcoma and carcinoma. Finally, the author points out that solid tumors can only be transformed into ascites tumors as long as the cancer cells retain their erythropoietic orientation.

- 63-313 ISOLATION OF GROWTH-PROMOTING SUBSTANCE(S) FROM CHICK EMBRYO EXTRACTS. (E.) Kuru, M. (Nat. Cancer Ctr., Tokyo), G. Kosaki and H. Watanabe. Gann 54(1):119-130, 1963.

A fraction which could be precipitated from crude saline extracts of 9-10-day-old chick embryos by addition of 30-70 % (v/v) ethanol was found to contain an oncotrophin-like substance or group of substances which stimulated the growth of strain L and Lp₁ cells in tissue culture. The active principle is non-dialyzable and is destroyed by heating at 100°C for 30 min. or by trypsin digestion; it is stable, however, to heating at 100°C for 5 min. or 56°C for 30 min. A nucleoprotein fraction obtained from the chick embryo extract by the method of Kutsky was ineffective in stimulating these tissue cultures, while the 30-70% ethanol fraction obtained from the nucleoprotein-free material was quite active.

- 63-314 ETIOLOGIC SURVEY OF CARCINOMA OF UTERINE CERVIX. (E.) She Ming-P'eng (Dept. Path., Inst. Exp. Med., Peking), Ch'eng Feng-Ling, Liu T'ung-Hua, Ts'ai Hai-Ying, Liu Chih-Ming and Wu Ai-Ju. Chin. Med. J. 82(1):39-45, 1963.

The results of a statistical survey showed a significant correlation among 278 pts. with cervical cancer (mostly squamous-cell), compared to 319 controls, and the factors of early marriage (48.5%:35.2%), early childbearing (28.0%:12.5%), multiple pregnancies (49.1%:35.4%), multiparity (43.0%:27.6%), frequent parturition (39.0%:22.7%), phimosis of partner (31.0%:11.7%), and emotional stress (47.5%:32.0%). Many carcinoma pts. had a combination of 2 or more endogenous and/or exogenous

factors, as compared to controls (67.7%:33.7%).

- 63-315 THE IMPORTANCE OF PENIS HYGIENE IN THE PREVENTION OF CERVICAL CARCINOMA. (Dut.) Kloosterman, G. J. (Amsterdam, The Netherlands). Nederl. T. Geneesk. 107(7):300-304, 1963.

Following a review of the literature describing statistical correlations between the incidence of cervical carcinoma and the sexual history of the pt. (age at marriage, number of pregnancies, frequency of intercourse, incidence of syphilis and gonorrhea, etc.), the author considers the role of circumcision of the male partner in more detail and briefly reports his own findings in 331 pts. with cervical carcinoma seen between 1959 and 1961. The group contained no virgins, 8.1% had more than 6 children, and 16% had salpingitis, gonorrhea or syphilis (compared to 30% in those who had never been pregnant and only 0.7% in the general hospital population). Since the incidence of penis carcinoma is also apparently affected by circumcision, he concludes that frequent intercourse with an uncircumcised, unhygienic male partner has a definite predisposing effect toward cervical carcinoma, possibly due to the presence of carcinogenic substances in the smegma. The author does not recommend routine circumcision, but emphasis on penis hygiene and routine cervical smears in those groups with the highest incidence of cervical cancer.

- 63-316 CARCINOGENIC ACTION OF HUMAN SMEGMA. (E.) Reddy, D. G. (Dept. Path., Andhra Med. Coll., Visakhapatnam, India) and I.K.S.M. Baruah. Arch. Path. (Chicago) 75(4):414-420, 1963.

Fresh human smegma was topically applied to the genital mucous membranes (vagina, cervix, penis, prepuce) and skin (back) of 29 male and 16 female albino Swiss mice (Rockefeller Inst. Lab. strain) 3 x/wk. for 16 mo. Almost 50% of the animals died of intercurrent infection before completion of the experiment. In 11 males, there was microscopic (but not gross) hyperplasia of the preputial epithelium, and in 5, of the penile epithelium, but these changes were benign. In 7 females, vaginal and cervical mucous membranes were hyperplastic, but not neoplastic. Skin changes of treated animals included hyperplasia of the hair follicles and of the basal epithelial cells in 4 that died early, and in animals that survived over 8 mo. there was atrophy of epidermis and hair follicles, with infection and ulceration in 5. In controls, 3 males and 2 females showed some skin atrophy, and 1 male slight hyperplasia. Slight ulcerations appeared in 2/10 male and 3/10 female controls. It is concluded, despite some of the conflicting reports of previous workers, that the carcinogenic potential of human smegma, if any, is very weak, and is subject to modification by the genetic constitution of experimental animals.

- 63-317 INDUCED HEREDITARY CHANGE IN DROSOPHILA BY INJECTED EXTRACTS OF NEOPLASTIC FLIES, MICE, OR HUMANS. (E.) Harnly, M. H. (New York U. Grad. Sch. Arts Sci.). Ann. N.Y. Acad. Sci. 100(Pt. 2):817-826, 1963.

Purified extracts prepared from either tu-e Drosophila larvae (a spontaneous hereditary melanotic tumor strain), tissue of spontaneous leukemic AKR and virus-induced leukemic C3H(f) mice, or serum from pts. with Hodgkin's disease were injected into 96 hr. larvae of the tumor-free wild 51-52 strain of D. melanogaster. In each experiment, the emerged adult hosts having melanotic tumors were then mated. In the F₃, 25% developed tumors, so that tumorous males could be selected and mated with virgin tumorous females, followed by virgin sib matings of tumorous flies for over 50 generations, by which time tumor incidence was increased to more than 90%. In a study of the mode of inheritance of these melanotic tumors, the results show no sex linkage or sexual dimorphism; the melanotic tumor phenotype appears to be due to a recessive gene at the tu-e locus in the right arm of the second chromosome. On the basis of a review of the other properties of these tumor-inducing extracts, the author concludes that these 3 and 29 similar extracts of malignant tissue all contain the same or very similar tumor-inducing entities.

- 63-318 UTILIZATION OF AN INDUCED DROSOPHILA MELANOMA IN THE STUDY OF MAMMALIAN NEOPLASIA. (E.) Kassel, R. (St. Vincent's Hosp., New York), L. Burton and F. Friedman. Ann. N.Y. Acad. Sci. 100(Pt. 2):791-816, 1963.

After describing the utility of the induction of melanotic tumors in Drosophila melanogaster as a rapid bioassay system for work with the tumor-inducing factor which can be obtained not only from Drosophila but from a variety of other neoplastic systems, the authors present the general results of 3 yr. work on the many factors comprising the tumor-inducing complex (TIC). In general, the TIC, which is obtainable from murine, human, fowl, insect and plant neoplasms and can produce tumors in both mice and Drosophila, contains a tumor factor (inactive stable component), an activator (inactive labile component, producing an active tumor-inducing agent when incubated with the tumor factor), an inhibitor which eliminates the activity of the activated tumor factor, a toxic factor and an antitoxic factor; the isolation and properties of these fractions are described in some detail, as well as some of the interrelationships between them when injected into mice or fruit flies. Particular attention is paid to the inhibitor system and its role in resistance to neoplastic disease, and experiments are reported in which balanced combinations of antitoxic factor and inhibitor were administered to mice with leukemia or mammary tumors, with marked tumor regression. In view of the complete lack of species specificity

in these factors, the authors postulate a general theory of carcinogenesis valid for all living organisms. It is not certain, however, whether the tumor-inducing complex and inhibitor systems act directly or via mediators such as viruses.

- 63-319 STUDIES IN CHORIOCARCINOMA FROM 88 PATIENTS ADMITTED TO THE PHILIPPINE GENERAL HOSPITAL FROM 1950-1961. (E.) Acosta-Sison, H. (Coll. Med., U. Philippines, Quezon City). *Acta Med. Philipp.* 19(2):77-83, 1963.

While frequency of choriocarcinoma increases after age 38 (25/88 in the present series), the largest number of cases occurred in the 21-30 age group (36/88) and 54/88 were under 36 yr. Seventeen (19.3%) had had one or two abortions, or hydatidiform mole (11/17) previous to the pregnancy that gave rise to the choriocarcinoma; and in 51/88, the pregnancy that gave rise to the choriocarcinoma was itself a hydatidiform mole. Except in 4 cases where choriocarcinoma followed a first pregnancy which ended in early abortion, the incidence according to gravity and parity ran parallel with the incidence of pregnancy. It is concluded that the normal chorionic cell degenerates and is absorbed or expelled after the death or expulsion of the fetus. The potentially malignant chorionic cell, which is malignant because of a defective gene, does not degenerate. It continues to live, either attached to the uterus or carried by the circulation to a distant organ, where it proliferates as a choriocarcinoma. The high incidence of these tumors in poor Oriental countries may be explained by their diet, which is markedly deficient in high quality protein.

- 63-320 STATISTICAL DATA AND CONSIDERATIONS ON THE CUTANEOUS TUMORS OBSERVED AT THE DERMATOLOGY CLINIC IN FERRARA BETWEEN 1956 AND 1961. (It.) Zavarini, G. (Derm. Clin., U. Ferrara, Italy). *Arcisped. S. Anna Ferrara* 15(6): 1187-1195, 1962.

Among 1055 pts. with cutaneous tumors seen at the Ferrara Dermatology Clinic (with incidence increased from 3.99% in 1956 to 10.08% in 1961), 645 had epithelial tumors (including 268 squamous cell, 253 basal cell, 62 papillomas), 105 had connective tissue lesions, 146 had precancerous states and 159 had nevi, for a total of 786 "cancerous" conditions. The incidence of cutaneous malignancy in Ferrara (131 carcinomas/yr. or 7.3% of all dermatologic pts.) is much higher than in other large Italian cities (128/yr. for Rome and 115 for Bologna but only 12 in Turin and 16 in Modena). The author suggests that this high incidence of skin cancer may be due both to racial factors and to environmental conditions (a primarily agricultural economy with high exposure to sunlight), leading to a high incidence

of senile atrophy, focal dyskeratosis and early connective tissue degeneration which reduce the defense mechanism of the body and open the way for the development of cutaneous malignancy.

- 63-321 MAST CELLS AND SUSCEPTIBILITY TO MAMMARY CANCER IN INBRED STRAINS OF MICE. (E.) Simpson, W. L. (Detroit Inst. Cancer Res., Mich.), Y. Hayashi and E. Pawley. Pp. 329-338 in *The Morphological Precursors of Cancer*. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

In an effort to determine the possible relationship of mast cell numbers to mammary cancer, it was determined that the mammary glands of 2-3-month old BALB/c mice (highly susceptible to milk agent) had fewer mast cells (70.5/mm²) than those of the resistant C57B1 strain (113/mm²), and that these numbers did not change markedly with age. Mast cell numbers in C3H/Sp (high cancer strain with milk factor) and C3H/AnSp (low cancer, without milk factor) mice were similar at 2-3-mo. (186.2 and 187.5/mm², resp.); however, at 5-6 mo., only the number in the former strain was elevated (257.3/mm²). It was also observed that in the milk agent carrying strain, with increasing age, there was a development of a greater number of ducts with more branching than in the strain not carrying the milk agent. The author concludes that there is highly significant correlation between the number of mammary gland ducts, the size of the ducts and the number of mast cells in the area. It is suggested that an increase in subepithelial mast cells may be one of the evidences of a localized preneoplastic condition.

- 63-322 THE OCCURRENCE OF LYMPHOMA IN PATIENTS WITH LONG-STANDING HYPERTHYROIDISM. (E.) Ulmann, J. E. (Dept. Med., Columbia U. Coll. Physicians Surg., New York), G. A. Hyman and B. Calder. *Blood* 21(3):282-297, 1963.

A group of 6 pts. (5 women, 1 man), with symptoms of lymphadenopathy, developed lymphomas (1 lymphoblastic lymphosarcoma, 1 Hodgkin's disease, 1 giant follicular lymphoma, 3 lymphocytic lymphosarcoma or lymphatic leukemia) at the age of 44-70 yr. following 7-45 yr. of active hyperthyroidism. Treatment, in most cases, was with partial thyroidectomy, iodides, propylthiouracil, radioactive iodine and/or methimazole; 4 of the pts. also had thyroid adenomas. Since hyperthyroidism in man seems to be associated with lymphocytosis and enlargement of lymphoid organs, and similar changes are produced by administration of thyroxine in animals, it seems likely that hyperthyroid may lead to lymphoid hyperplasia and malignancy.

- 63-323 GLYCOLYSIS BY SUBCELLULAR MELANOMA FRACTIONS AND THE EFFECTS OF INSULIN, ENDOTOXIN, AND TESTOSTERONE. (E.) Giger, K. (NCI, Bethesda). *Ann. N.Y. Acad. Sci.* 100 (Pt.2):866-875, 1963.

Studies of anaerobic glycolysis in centrifugal fractions from sucrose homogenates of S91 mouse melanoma showed that about 40% of the glycolytic activity of cleared homogenates was associated with a particulate "mitochondrial" fraction and that this activity could be stimulated *in vitro* by insulin or a polysaccharide endotoxin from *Serratia marcescens*, but was inhibited by testosterone propionate; the effects of low concentrations of insulin and endotoxin were additive. All of the hormonal effects could be attributed to the effects on the hexokinase reaction.

63-324 ETHNIC DIFFERENCES IN SKIN CANCER IN HAWAII. (E.) Quisenberry, W. B. (Hawaii State Dept. Health, Honolulu). Nat. Cancer Inst. Monogr. (10):181-189, 1963.

In Hawaii, the main ethnic groups are: Caucasians, 22%; Japanese, 32%; Hawaiians and part-Hawaiians, 44%. The rate of skin cancer, based on hospital records (per 100,000: males, 1991 cases; females, 1680 cases) for the 3 groups, were, resp.: 12.7 and 6.1; 2.2 and 0.8; 0.6 and 1.4. Rates (male and female) for Chinese were 3.0 and 1.6; for Filipinos 1.2 and 0.7. In 61% of pts., the lesions were on face or head, and in 18% on the extremities. Most were squamous-cell or basal-cell carcinomas. Melanomas were not included in the study. In another study (Honolulu County, 1955-1956), of 293 reported skin cancer cases, for 276 Caucasians, the rate was 138; for 9 Japanese pts., 1.5; and for 2 Hawaiians, 1.6. The head and face were most frequently involved. The skin pigmentation of the non-Caucasian groups is probably the most important factor in the lower incidence. However, the high incidence of skin cancer in Hawaii's Caucasians is attributable to the low latitude, with consequent increase of UV irradiation and to the continued exposure to this possible carcinogen with no winter "rest" period.

63-325 SKIN CANCER IN NEW GUINEA NATIVE PEOPLES. (E.) Atkinson, L. (Dept. Path., U. Western Australia Med. Sch., Perth.), Farago, B. R. V. Forbes and R. E. J. ten Seldam. Nat. Cancer Inst. Monogr. (10):167-179, 1963.

Skin cancers diagnosed among the deeply pigmented native population of the Australian part of New Guinea in 1958-61 totalled 99 (67 histologically confirmed) included: 90 squamous-cell carcinoma, 5 basal-cell carcinoma, and 5 malignant melanoma. Most lesions (71) were located on the leg and foot. Metastases had already developed in 20% when first seen. Etiologic factors included sunlight, traumatic scars, and chronic tropical ulcers. There appeared to be no connection with the after-effects of yaws (scars and deformations).

63-326 A STATISTICAL STUDY ON MALIGNANT TUMORS OF THE BLADDER IN THE PADUA DISTRICT. (It.) Lippi, U. (Inst. Anat., U. Padua, Italy)

and F. Callegari. Riv. Anat. Pat. Oncol. 21(6): 931-954, 1962.

A review of the 18,797 autopsies performed in the Padua district between 1907 and 1958 revealed a total of 143 bladder malignancies (48 primary and 95 secondary), with a gradually increasing incidence which could be ascribed to improved diagnostic facilities. The 48 primary cases included 43 males and 5 females. In male pts. with primary tumors, 25.6% occurred between 40-55 yr., 50.5% between 55-75 yr.; the female primary tumors occurred above age 60. As to tumor type 68% were papillary, and 32% were of the infiltrating type, either ulcerative or non-ulcerative, affecting mainly the trigone but also the posterior and lateral walls. Among the 95 cases with secondary bladder malignancy, 28 were males and 67 females. The maximal incidence was at 60-75 yr. in males, but at 40-50 yr. in females. The primary tumor was in the uterus in 48 of these 95 pts., in the prostate in 14 and in the rectum in 10. These data are compared with data from the literature.

63-327 MASTOPATHY AS PRECURSOR OF CANCER OF THE BREAST. (E.) Bahrmann, E. (Friedrichshain Hosp., Berlin). Pp. 395-403 in The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Examination of 500 resected mammary carcinoma specimens, revealed 44% with undoubted mastopathy, 22% with adenofibrosis. Other workers have found, statistically, a $2\frac{1}{4}$ - to $5\frac{1}{2}$ fold greater risk of cancer in persons with a history of mastopathy than in the general population. The histological findings in mastopathy, particularly the proliferation centres described by Semb (solid epithelial nests among sparse lactiferous ducts in hyalinized centers, with proliferation of elastic tissue, while glandular elements with cysts and papillomata radiate in all directions) form a particularly convincing bridge to breast cancer. These centers may be multiple, and may be found in different stages of development.

63-328 INTERRELATIONS BETWEEN CANCER AND TUBERCULOSIS OF THE LUNGS. (E.) Kheifets, S. L. (Oncol. Stat. Oktyabr' Dist., Leningrad). Fed. Proc. 22(2) (Pt.2):T383-T384, 1963. (Transl. from: Klin. Med. (Moskva) 40(6):39, 1962.)

A study of the case histories of 216 pts. (177 men and 39 women) with fatal lung cancer revealed reliable evidence of associated tuberculosis (TB) in 67 cases (54 men and 13 women); in 21 to these there was active or inactive TB; there was coincidence of location of the cancer in 16. In 14/67 there was calcification, again usually at or near the site of the tumor. In 13 other cases, bronchoscopy or histological study revealed scars or fresh adenobronchial perforations; finally, in 19 peripheral tumors were found which had developed on the basis of subpleural scars and pleuropneumoscrosis. In addition, 20 other pts., who did

not show clinical or morphological signs of TB, nevertheless either had a history of TB in their medical records (8 cases) or had recovered from exudative pleuritis (12 cases). On the basis of these findings and a review of the literature, the author concludes that TB is one of the etiological factors in the development of cancer of the lung.

- 63-329 FACTORS AFFECTING SURVIVAL OF PATIENTS WITH OVARIAN CARCINOMA. (E.) Stone, M. L. (Dept. Obstet. Gynec., New York Med. Coll.), A. B. Weingold, S. Sall and B. Sonnenblick. Surg. Gynec. Obstet. 116(3):351-360, 1963.

Among 223 pts. with confirmed ovarian carcinoma, 131 were treated prior to 1956. There were 27 5-year survivors (20.6%). There was no significant correlation between survival and duration of symptoms (most less than 1 yr., average, 4 mo.); type of pathology (seroanaplastic, undifferentiated cystadenocarcinoma); nor type of symptoms (bleeding, pain, g.i. disturbances, palpable mass). Survival was higher for pts. with granulosa cell tumors (50%) and where abnormal bleeding was the presenting symptom (40%). Five-year survival, where disease was localized to the ovary (33 pts.), was 57.5%; in 11 with regional tumors, 18.1%; and of 81 pts. with remote disease, 6.1%. The various surgical and radiological therapies carried out could not be definitely correlated with survival. Survival was negatively correlated with age (47.3% for pts. under 40 yr. and 16.1% for those over 40). Five-year survivals were 23.5% for the 102 married pts., 10.3% for the 29 unmarried; and 24.3% for the 31 multiparous pts., 16.9% for the 100 nulliparous pts.

- 63-330 CANCER OF THE STOMACH SEEN AT UNIVERSITY COLLEGE HOSPITAL, IBADAN. (E.) Elebute, E. A. (Univ. Coll. Hosp., Ibadan, Nigeria), V. A. Ngu, A. R. Mainwaring and R. C. Eruchalu. West Afr. Med. J. 12(1):11-17, 1963.

Among 86 Nigerian pts. with carcinoma of the stomach (62 males, 24 females) seen between April 1957 and December 1961, age distribution showed a peak between 40-50 yr. (approximately); blood group distribution followed that of the general population. The most favored site was the pyloric antrum (74%). The incidence of gastric carcinoma at this hospital was 2/1000 admissions; in a 2-year period, gastric carcinomas constituted 2.54% (45/1372) of malignant tumors diagnosed by the Pathology Dept. Comparison of these figures combined with autopsy data suggest that gastric carcinoma is fairly common among Africans, and may be as common as among Europeans.

- 63-331 SMOKING AND LUNG CANCER. (E.) Harvey, C. Aust. Nurses J. 61(3):62-64, 1963.

A general restatement of the strong statistical

evidence for an etiologic relation between cigarette smoking and lung cancer, with a plea for a campaign against smoking.

- 63-332 SEX CHROMATIN AND PRECANCEROUS AFFECTION OF THE BREAST. (E.) Bullón, A. (Inst. Morbid Anat., U. Seville, Spain) and C. Barrio. Pp. 375-382 in The Morphological Precursors of Cancer. Severi, L. (Ed.) Perugia, Div. Cancer Res., 1962.

Sex chromatin in the resting nuclei of all normal tissues from females was also present in their benign tumors (Barr-positive). In other conditions, percentage of Barr-positive tissues was: cystic mastopathies 70.6%; malignant tumors (39 breast cancers) 48.7%. Average percentages of Barr-positive cells were: in normal tissues 73.5; in benign tumors 74; malignant tumors 69; and cystic mastopathy 70.17. Cells lacking sex chromatin seemed to have well developed nucleoli, and vice versa. In a case which presented both mastopathy and carcinoma in the excised breast, the Barr number for the former was 22%, the latter 20%, and stroma 86%. A pt. with mastopathy and a Barr number of 21% in the epithelium and 71% in the stroma, was followed and 1½ yr. later had a carcinomatous recurrence. On radical mastectomy there were found coexistent malignant zones with Barr numbers of 37% in the epithelium and 76% in the stroma; zones of adenoma fibrosum had a Barr number of 82%.

- 63-333 PREMALIGNANT CHANGES OF CERVICAL CARCINOMA STUDIED WITH SIMULTANEOUS COLPOSCOPIC AND CYTOLOGIC EXAMINATIONS. RESULTS OBTAINED IN 8,000 CASES. (E.) Bacaj, T. (Alexandria Hosp., Alexandria, Va.), P. Fioretti and G. Valle. Pp. 489-502 in The Morphological Precursors of Cancer. Severi, L. (Ed.) Perugia, Div. Cancer Res., 1962.

Among 7,996 adequate vaginal smears made routinely from hospital and clinic pts., 82.31% were negative (Pap I); 13.89% nuclear hyperactive (Pap II); 2% suspicious (Pap III); and 1.7% positive (Pap IV and V). In cases with proven cancers, there were only 4.3% false negatives (1 preinvasive squamous cell carcinoma of the cervix and 7 adenocarcinomas of the endometrium). Positive smears were found in 111/186 cancers. An additional 49 were suspicious, and 18 were nuclear hyperactive. The distribution of types was: invasive squamous-cell carcinoma of the cervix, 109; preinvasive, 37; adenocarcinoma of the cervix, 9; of the endometrium, 31. Among "suspicious" smears, 53/167 proved to be uterine carcinomas (31%); likewise 118/136 positive smears were confirmed with only 18 false positives (14%). Colposcopic examination of 8000 cases revealed 38.8% normal; 41.8% ectropion and ectopy; 16.1% transformation zone; 4.6% cervical polyps; 7.3% senile atrophic colpitis; 18.9% Trichomonas colpitis; 9.4% Candida colpitis; and 4.9% non-specific bacterial colpitis. Diagnostic accuracy of cytology was 97%, of colposcopy 92%. Some of the changes detected may be morphologic precursors of cancer, others true, though asymptomatic malignancies.

63-334 RELATIVE INCIDENCE OF SKIN CANCER IN CHINESE IN TAIWAN: WITH SPECIAL REFERENCE TO ARSENICAL CANCER. (E.) Yeh, S. (Dept. Path., Nat. Taiwan U. Coll. Med., Taipei, China). Nat. Cancer Inst. Monogr. (10):81-107, 1963.

Of the 12,084 malignant tumors found among 100,554 surgical specimens, 563 (4.65%) were skin tumors (282 carcinomas of skin, and 281 sarcomas, malignant melanomas, and carcinomas of lip, penis and vulva). Of the 489 carcinomas listed, 385 were epidermoid, 58 basal-cell, 35 intraepidermal (Bowen's disease), 8 adenocarcinomas and 3 carcinosarcomas. A study of 4000 autopsies included 570 (14.25%) malignant tumors, of which 13 were skin carcinomas or anatomically related malignancies. The skin cancer incidence reported (1.02%) is much lower than any necropsy data from the USA. While most numerous in the 6th decade, skin cancers increased steadily (proportionally) up to age 80. Carcinoma of the penis, constituted 0.84% of all tumors (2.2% of all cancers in males), and 100/101 were epidermoid, a majority occurring in men over 40. The authors suggest that phimosis and bad personal hygiene may be etiological factors in penile cancer. Malignant melanomas (44) were found in 0.08% of all autopsies (0.52% of all tumors). Arsenical skin cancers were found in 52 pts. (32 males, 20 females) of a population of approximately 160,000, who lived in a limited area where the arsenic content of the drinking water is 0.8 to 2.5 ppm.; 73.1% occurred at ages over 50. Skin lesions were seen in 81.8% of pts. with blackfoot (which appeared to be closely associated with chronic arsenical intoxication); 1% had carcinoma. From a study of 94 exposed for varying periods of time, hyperpigmentation was found only in persons exposed at least 5 yr., keratinism 15 yr., cancer 20 yr. Some pts. developed cancer 30 to 40 yr. after use of the contaminated water was discontinued.

63-335 REGIONAL INCIDENCE AND PATHOLOGY OF SKIN CANCER IN THAILAND. (E.) Tansurat, P. (Siriraj Hosp., Bangkok, Thailand). Nat. Cancer Inst. Monogr. (10):71-74, 1963.

A group of 11,080 surgical cancer specimens from a Bangkok hospital (1949-1960) included 1,020 skin cancers (9.29%). The highest incidence was in the sixth decade. Male:female ratio was 3:2, and frequency was much greater in Thai pts. than in Chinese (9:1). The predominant skin cancers were: squamous-cell carcinoma (663); basal-cell carcinoma (210); malignant melanoma (55); and undifferentiated carcinoma (26). Squamous-cell carcinoma constituted 70% of all skin cancers and occurred most frequently on the head (30.3%), penis (25.6%), legs (13.6%), and vulva (11.2%). Among 55 cases of malignant melanoma, 17 occurred on the head and neck, 10 on the upper limb, 15 on the lower limb, 11 on the trunk. Of the 15 cases on the lower limb, 9 were on the sole of the foot of pts. who usually went barefooted. Predisposing factors listed included exposure to sunlight,

chronic ulceration, trauma, and poor personal hygiene. Age and occupation are also mentioned as possible factors.

63-336 SKIN CANCERS IN JAPAN: A NATIONWIDE 5-YEAR SURVEY, 1956-1960. (E.) Miyaji, T. (Osaka U. Med. Sch., Japan). Nat. Cancer Inst. Monogr. (10):55-71, 1963.

A survey at 41 university hospitals, which included reviews of histologic sections of biopsies (851,685 first dermatological visits), showed the incidence of primary skin carcinoma in Japan to be 0.10%, lower than the rate for Austria (2.1%) or the U. of Colorado (15.3-17.5). Classified histologically, the most prevalent types (male-female) were epidermoid carcinoma (317-224) and basal-cell carcinoma (106-94); occurrence was most frequent in the seventh decade. Body sites most frequently affected were the scalp and face for both squamous-cell (541) and basal-cell (200) carcinoma cases. Paget's disease (51 cases) was distributed in the area of the genitalia, Bowen's disease (35 cases) was evenly distributed, as was also cutaneous sarcoma (60 cases). Malignant melanoma (81 cases) was more or less localized in the trunk. Other data collected included: mean duration of preceding diseases before apparent malignant changes; (6 mo. to 12 yr.); precancerous lesions; and occupational factors. The incidence of malignant changes in precancerous dermatoses was, for xeroderma pigmentosum, 15.8%; chronic ulcer, 11.8%; radiodermatitis, 10.5%. Among pts. exposed to sunlight (outdoor occupations), more developed carcinoma than sarcoma. Plotted geographically, skin cancer incidence was higher (equal to or greater than 2/1000 first dermatologic visits) in the South and West, where there was more sunlight, than in the North and East (less than 1/1000).

63-337 EPIDEMIOLOGY OF SKIN CANCER IN NEW ZEALAND. (E.) Eastcott, D. F. (48 Cuba Street, Petone, New Zealand). Nat. Cancer Inst. Monogr. (10):141-151, 1963.

A retrospective study of skin cancer cases in New Zealand showed incidence rates of 5 per million, (male and female) at age 25; approximately 80 male and 50 female at age 35; 300 and 100 at 55; and 500 and 200, resp., at 65. For males the rate is 5-6 times, and for females, 2-3 times the French rate. Estimated total yearly rates of skin cancers were: malignant melanoma 55; basal-cell carcinoma 1,130; and squamous-cell carcinoma 380. Malignant melanoma, while much higher than in Britain and the USA, was not as high as in Australia. Basal-cell carcinoma was more prevalent in New Zealand than in Britain, and higher than in Australia, the highest frequency was on the head and neck. The prime etiologic agent seemed to be sunlight, especially among fair-skinned persons. The distribution pattern of facial sites, concentrated near sebaceous glands, and the overall high incidence in New Zealand, with its high

dietary animal fat intake, might be accounted for by the assumption that, where fatty material is concentrated, sunlight acts upon some skin precursor (like that for Vitamin D) to render it carcinogenic. A high frequency of chronic lymphatic leukemia was found among males with basal-cell and squamous-cell carcinoma (6/446, expected incidence, 0.2/446).

- 63-338 SOME EPIDEMIOLOGICAL FEATURES OF BREAST CANCER AMONG MALES. (E.) Schottenfeld, D. (Dept. Chronic Dis., Johns Hopkins Sch. Hyg. Pub. Health, Baltimore, Md.) and A. M. Lilienfeld. *J. Chronic Dis.* 16(1):71-81, 1963.

The age specific mortality rates for male whites and non-whites with breast cancer in 1939-41 and 1949-58 are presented, showing an exponential increase with age but a slight decrease for whites over the 20 yr. period. Geographical variations in the incidence of breast cancer in the USA are also discussed, showing a lower incidence in the South, as well as some international comparisons which indicate very low rates in Finland and Japan. Other factors which should be considered are marital status and religion, since the mortality rates are particularly high in Jews and in divorced or widowed men of all religions.

- 63-339 EFFECTS OF PIGMENT ON BOVINE OCULAR SQUAMOUS CARCINOMA. (E.) Anderson, D. E. (Dept. Biol., U. Texas M. D. Anderson Hosp., Houston). *Ann. N. Y. Acad. Sci.* 100(Pt. 1): 436-446, 1963.

A statistical survey of some 45 herds in 23 states in the USA and Canada (7500 animals) revealed an inverse correlation between pigmentation and susceptibility to cancer of the bovine eye. Thus, the number of lid lesions in animals with pigment over less than 50% of the lid length exceeded the number expected, while no lesions were observed in completely pigmented lids. In contrast, however, there is no correlation between lid pigment and lesions at the corneoscleral junction, which are also apparently inherited and are affected by the pigment in the bulbar conjunctiva. Similarly, lesions on the nictitating membrane are influenced by its pigmentation. Thus, phenotypic selection for increased ocular pigment would probably decrease the incidence of bovine ocular cancer. Possible correlations between ocular cancer and other factors, such as age, nutrition and sunlight (whether measured by latitude, annual hours of sunshine or altitude), are also reviewed. The author concludes that the correlation between pigmentation, which is hereditary, and cancer may explain the apparent

genetic basis for susceptibility to bovine ocular cancer.

- 63-340 STUDIES IN ORAL CANCER EPIDEMIOLOGY. 2. FREQUENCY OF ORAL CANCER. (E.) Pindborg, J. J. (Dept. Oral Path., Royal Dent. Coll., Copenhagen.). *J. Dent. Res.* 42(1)(Pt. 2): 348-352, 1963.

A statistical study of comparative morbidity and mortality due to cancer of the lip, tongue, salivary glands, mouth and pharynx (tonsils) in various countries showed that oral cancer accounted for 6.2% of all male cancers and 1.9% of female cancers in the USA (1947), with generally lower percentages for other countries, and that the male Caucasian population of the USA had the highest morbidity rate (21.1/100,000), with markedly lower rates for other countries and consistently lower rates for females and non-Caucasians. The most common sites for oral cancer were the lip in males (Caucasian) and the salivary glands in females. Oral cancer mortality in the USA ranks below Ireland, France, Switzerland and the U.K. for the male Caucasian population and even further down for females and non-Caucasians. Generally, mortality rates from oral cancer have decreased in recent yr., although the morbidity, at least in Denmark, has remained constant. Some of the decrease might be related to present-day better oral hygiene.

- 63-341 THE RELATION OF RACE AND COMPLEXION TO THE INCIDENCE OF MOLES AND MELANOMAS. (E.) Pack, G. T. (Mem. Hosp. Cancer Allied Dis., New York), J. Davis and A. Oppenheim. *Ann. N.Y. Acad. Sci.* 100(Pt. 2):719-742, 1963.

In an extensive review of the literature (39 references), and after consideration of some personal contributions, it is concluded that melanomas tend to occur following excessive exposure to sunlight in fair skinned persons whose skins lack the capacity to respond by formation of melanin. This is confirmed by data on the complexion of pts. with melanoma compared to other cancer pts., the occurrence of freckles and tanning in melanoma pts., the incidence of melanoma in albinos (who do not lack melanoblasts but have negative dopa and tyrosinase reactions) and the development of melanoma in gray Percheron horses. Also discussed is the comparative frequency and distribution of nevi in various racial groups, including the Mongolian spot, blue nevi and the nevus of Ota. A detailed analysis is made of the occurrence of malignant melanoma in the Negro, with particular attention to data on the anatomical sites, age and sex distribution, preexisting nevi and the relative degree of malignancy.

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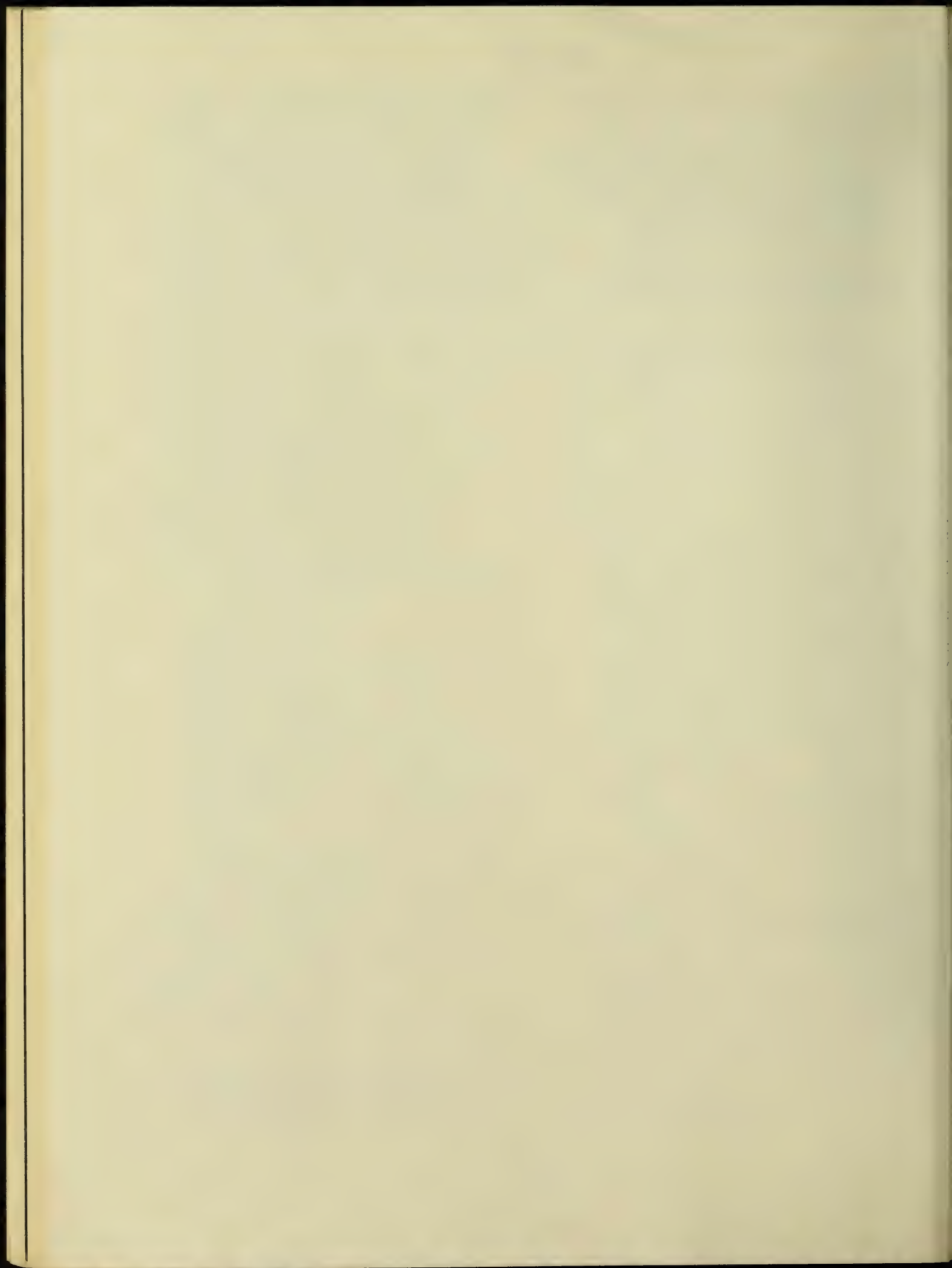
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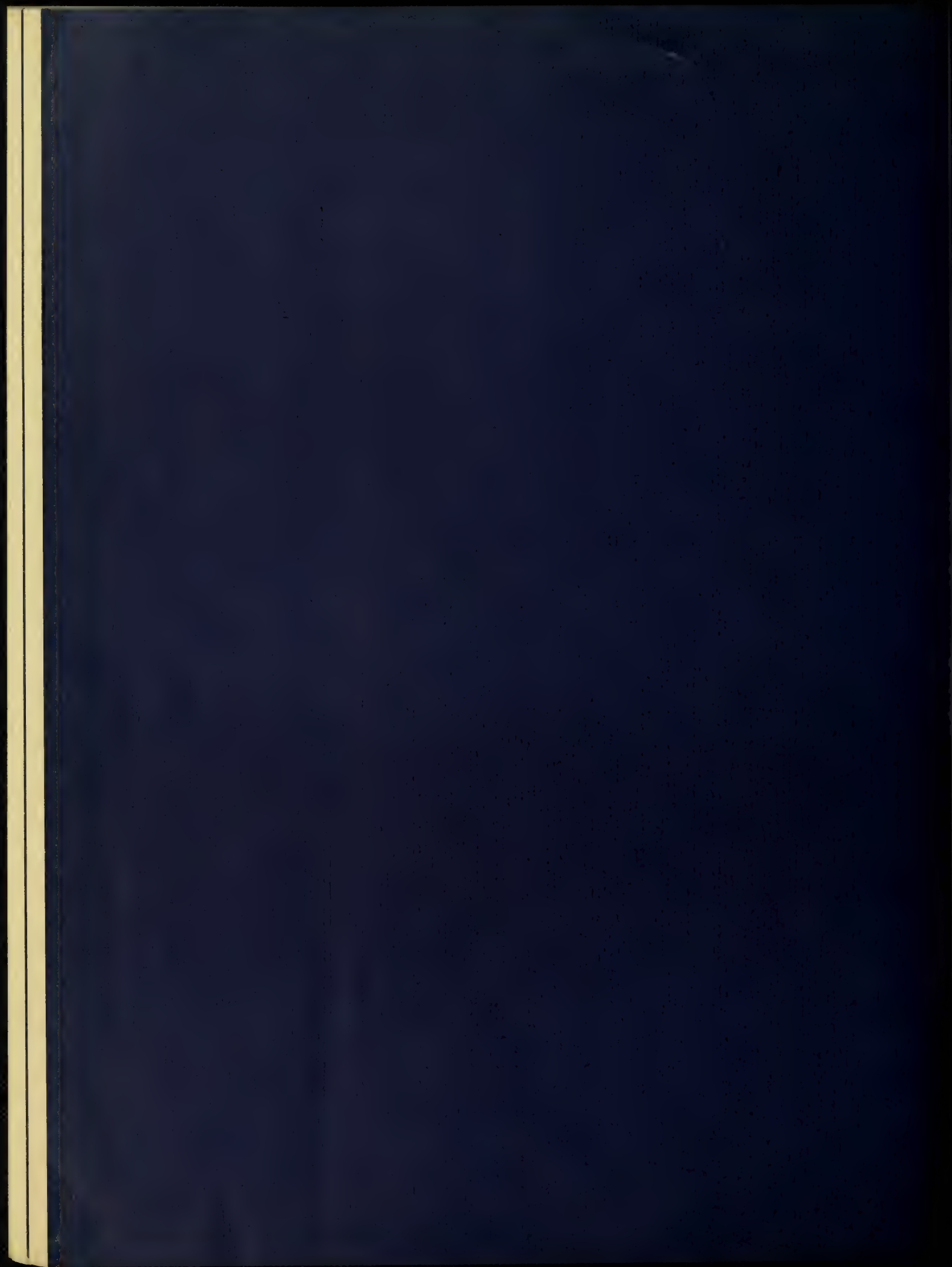
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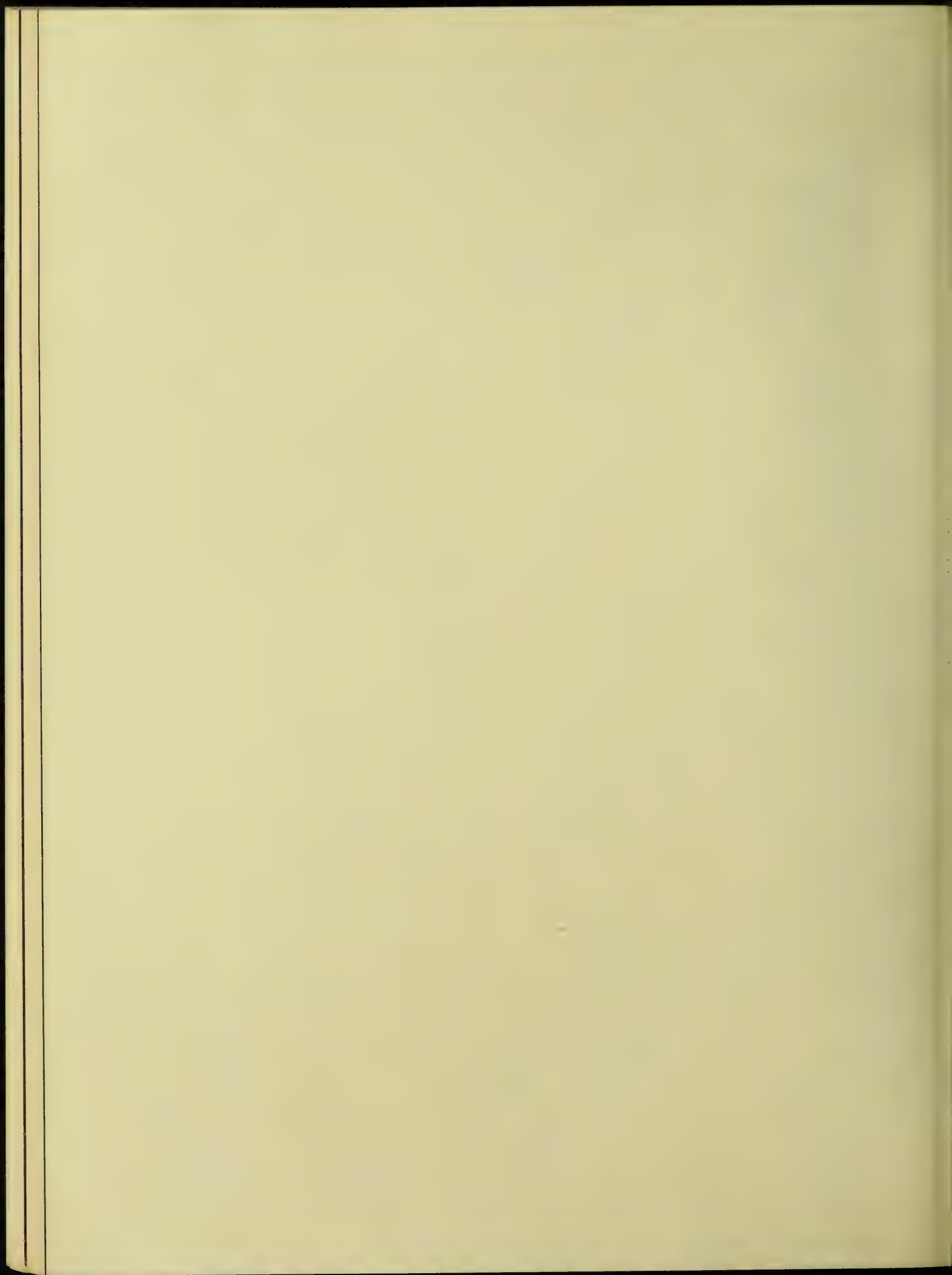
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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

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Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NIH	National Institutes of Health, USA
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	QO ₂	oxygen quotient
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FFU	focus forming unit	pt.(s)	patient(s)
g.i.	gastrointestinal	RBC	red blood cells (erythrocytes)
g	gram(s)	RES	reticuloendothelial system
μg	microgram(s)	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
i.a.	intra-arterial	RNase	ribonuclease
LD ₅₀	median infectious dose	soln.	solution
inj.	injected, injection(s)	s.c.	subcutaneous
inoc.	inoculated, inoculation(s)	TCID	tissue culture infectious dose
i.p.	intraperitoneal	x	times (e.g. x 3/wk.)
I.U.	international unit(s)	U	unit
i.v.	intravenous	UV	ultraviolet
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose	VA	Veterans Administration
M	molar, mole(s)	wt.	weight
mM	millimole(s)	WBC	white blood cells (leukocytes) or white blood cell count
μM	micromole(s)		
max.	maximum	yr.	year(s)

LANGUAGE ABBREVIATIONS

Af.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

- 63-342 A RECONSIDERATION OF THE PATHOLOGY OF PAGET'S DISEASE OF THE NIPPLE. (E.) Orr, J. W. (Dept. Path., U. Birmingham, England) and D. J. Parish. Pp. 429-433 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Based on a histopathologic review of 30 cases of Paget's disease, it is suggested that while the endogenous carcinogenic agent responsible for the disease is also probably the one which causes the deep mammary gland carcinoma which always accompanies or follows it, the Paget skin change is not necessarily cancerous. The epidermal cells adjacent to the large Paget cells regularly become depigmented. The destruction of the nipple is a consequence of subepidermal inflammation and degeneration, not of infiltrative invasion from the epidermis. This continuous process of damage and reaction implies the constant effective presence of the etiologic agent. (9 references)

- 63-343 FACTORS DETERMINING THE NEOPLASTIC RESPONSE INDUCED BY CARCINOGENS. (E.) Shubik, P., G. Della Porta, G. Pietra, L. Tomatis, H. Rappaport, U. Safflotti and B. Tóth. Pp. 285-297 In Biological Interactions in Normal and Neoplastic Growth. Brennan, M. J. and W. L. Simpson (Eds.). Boston, Little, Brown and Co., 1962.

In a general review and analysis of their own previously published work with the Syrian hamster, the authors summarize the incidence of various types of tumors in animals admin. a variety of carcinogenic agents, and attempt to draw some unifying conclusions. Liver tumors seemed to be favored particularly by oral 2-acetylaminofluorene (AAF; cholangiomas), CCl₄ (carcinomas) or *p*-aminoazotoluene (AZT; varlous). A high incidence of skin tumors appeared after cutaneous or endotracheal application of 9,10-dimethyl-1,2-benzanthracene (DMBA), as well as after oral urethan (U) or 20-methylcholanthrene (20-Me); the first 2 agents also favored the appearance of respiratory tract tumors. Tumors of the g.i. tract appeared after endotracheal DMBA or oral U, 20-Me, AZT, 4-dimethylaminoazobenzene or AAF. In addition, some of these carcinogens favored the appearance of lymphomas, hemangiomas and/or hemangiosarcomas, and particular interest is attached to the induction of mammary carcinoma and tumors of the thyroid, adrenal and ovary by carcinogens such as DMBA, U, 20-Me and AZT. The authors conclude that carcinogens may exert 3 types of action: they may, as in the case of AAF, merely increase the incidence of tumors also seen in controls; they may, as does CCl₄, induce a specific type of tumor in a particular organ; or they may have both effects (U and AZT). The complexity of such studies are stressed. (19 references)

- 63-344 CARCINOGENESIS IN RELATION TO THE FUNCTION OF ENDOCRINE ORGAN TRANS-PLANTS. (E.) Mühlbock, O. (Netherlands Cancer Inst., Amsterdam) and L. M. Boot. Pp. 255-260 In Biological Interactions in Normal and Neoplastic Growth. Brennan, M. J. and W. L. Simpson (Eds.). Boston, Little, Brown and Co., 1962.

Briefly reviewed is the authors' own transplantation studies with ovarian and pituitary tissue in inbred animals. This type of dislocation gives rise to neoplastic changes in the transplanted organ in both cases, so that analysis of the hormonal interplay may well be of interest from the point of view of causative factors in carcinogenesis. Ovarian transplantation into either the spleen, the anterior chamber of the eye or s.c. is first discussed, and the results (tumor frequency) is seen to be dependant upon the strain of mice; this dependence may be due to variation in susceptibility of ovarian tissue to gonadotropic hormones. The formation of mammary carcinoma or pituitary adenoma after isografting of pituitary glands into otherwise normal female mice is discussed. While the mammary tumors are due to the continual release of prolactin from the transplanted pituitary (which is not under hypothalamic control), the role of hormones in the etiology of the pituitary adenomas is not established, although the lack of hypothalamic inhibition probably has an effect. Some of the other factors (genetic constitution, age and sex) entering into these relationships are pointed out. (No references)

- 63-345 ENZYMATIC DETERMINATION OF TRANSMISSIBLE REPLICATING FACTORS ASSOCIATED WITH MOUSE TUMORS. (E.) Riley, V. (Sloan-Kettering Inst., Rye, N. Y.). Ann. N. Y. Acad. Sci. 100(Pt. 2):762-790, 1963.

A detailed review of both his work and the literature is presented of a new virus-like agent or agents from transplanted mouse tumors, the principal effect of which is to increase the plasma lactic dehydrogenase (LDH) activity of the infected host. The characteristics of these factors and the technics by which they can be detected and studied are discussed. Although the agents are transmissible and replicating and are inactivated by heating (100°C for 10 min. or 60°C for 40 min.), their extremely small size and resistance to DNase or RNase may indicate that they differ from classical viruses. The agents are associated with a wide variety of transplanted mouse tumors (carcinomas, sarcomas, leukemias and others), but are not found in primary tumors induced chemically or by radiation, nor in transplanted tumors in rats or hamsters. Following administration of tumor or organ extracts or blood plasma from tumor-bearing mice, by practically any route or topically to the skin, the plasma LDH activity rises to a plateau which persists for the life of the animal and corresponds to the level attained after disappearance of a surgically

or chemically treated tumor (5-10 times the normal level); in the presence of a growing tumor, however, there is a further marked elevation in LDH activity (up to 10 times the previous plateau). These virus-like agents also have a synergistic effect on other tumors, such as 20-methylcholanthrene-induced sarcomas, which do not contain such agents, resulting in increased tumor size and more severe host anemia. After inoculation of Cloudman S91 melanoma (i.m.) in different hybrid mouse strains of both sexes, males were found to be more susceptible; the genetic traits of the DBA strain were found to favor tumor growth, but were not absolutely necessary for it (some growth in Swiss X C57BL/6). In addition to producing anemia in the host, these agents increase the severity of splenomegaly, and seem to stimulate tumor cell glycolysis. While the etiological role of these virus-like agents is unknown and difficult to establish, they certainly have an effect on the course of the malignant process. (30 references)

- 63-346 STUDIES ON THE REPLICATION AND PROPERTIES OF THE BITTNER VIRUS. (E., Abstract) Moore, D. H. (Rockefeller Inst., New York). Pp. 16-17 in Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M. D. Anderson Hosp., Houston, February 20-22, 1963.

Reviewed are some of the recent experimental findings which have contributed to the positive identification of the B particles as the milk agent; it is concluded that the only negative argument is the occurrence of these particles in some tumors which lack biological activity. For example, the mammary carcinomas developing in a small percentage of high-cancer-strain mice which have been foster-nursed on agent-free mothers contain a small number of B particles but no biologically active milk agent. This lack of activity is thought to result from inhibition of the low yield of B particles by the large numbers of other particles, although it may also be due to inhibition by non-particulate substances or defects in the B particles themselves. One other problem considered is the production of mammary tumors in low-cancer-strain mice by hormonal stimulation (e.g. hypophyseal transplantation); this was found to be impossible in a highly susceptible line of C57 mice which was definitely free of the mammary tumor agent, so that again, a low concentration of B particles seems to be necessary. The addition of extra pituitary tissue can then overcome the particle deficiencies and/or suppressors and permit tumor development.

- 63-347 "NEWER" AND "OLDER" VIRUSES IN MAMMALIAN MALIGNANCY. (E., Abstract) Hilleman, M. R. (Merch Inst. Therapeut. Res., West Point, Penna.). Pp. 41-42 in Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M. D. Anderson Hosp., Houston, February 20-22, 1963.

In a brief review of recent developments in the study of oncogenic viruses, the author emphasizes the ordinary nature of most oncogenic viruses, which seem to cause ordinary necrotic-type cellular damage much more frequently than induce proliferative lesions. Some of the technics by which more human oncogenic viruses may be isolated are discussed, including *in vitro* tests for malignant cell transformation, cell chromosome alteration and mitotic stimulatory capacity, *in vivo* animal tests and controlled clinical studies such as those suggesting that rubella, mumps and various other viruses are implicated in human malignancy (presumably as an extrinsic source of abnormal genetic material). The importance of epidemiological studies and the possibilities of immunological control of human cancer are stressed. There is now suggestive evidence that certain cases of leukemia may follow infectious disease processes; African lymphoma appears to be mosquito-borne, perhaps in a way similar to rabbit myxoma virus.

- 63-348 VIROLOGY AND IMMUNOLOGY OF CANCER. (Rus.) Zil'ber, L. A. and G. I. Abelev. Moscow, Gosud. Izdat. Med. Liter., 1962, 455 pp.

In an extensive monograph, in which the authors review the detailed results of their own work and that of numerous other Soviet and non-Soviet investigators in 2 important aspects of oncology, i.e. the role of viruses in the etiology of cancer and the immunological characteristics of malignant tissue, they present, for the first time, a systematic exposition of the viro-mutational theory of carcinogenesis. After discussing the different theories of carcinogenesis, they describe the morphology and immunological properties of most of the known tumor viruses (viruses of chicken and mouse leukemia, polyoma virus, Rous sarcoma virus, the milk agent, papilloma virus and possible human tumor viruses), and review experiments on masked viruses, and latent tumor viruses, the adsorption of tumor viruses by erythrocytes, the pathogenic potential of tumor viruses and the conditions under which pathogenic properties are manifested, and the mode of transmission of tumor viruses. In arriving at a general conclusion as to the mechanism of carcinogenesis, the authors report some of their own recent work with polyoma virus growing in hamster embryo cultures. This showed that virus could be detected only during the first 4 weeks after inoc., even though the morphological changes in the cells and their vigorous reproduction continued; moreover, tissue removed 14 weeks after inoc., when no virus could be found, produced s.c. carcinomas or angioendotheliosarcomas in young hamsters, but the animals did not develop viral antibodies. Once transformed, the malignant hamster cells were resistant to reinfection with polyoma virus, even after irradiation. On the basis of this work and other work in the recent literature, the authors conclude that tumor viruses produce a hereditary malignant change in the host cell, due to the incorporation of viral DNA into the genome, after

which the virus disappears and is no longer necessary for the further development of the tumor. They draw an analogy between the production of malignant change of cells by tumor viruses and the lysis of bacteria by bacteriophage, and suggest that the clinical manifestations of this neoplastic transformation depend on a variety of environmental factors. They emphasize, however, that the various carcinogenic factors which have been implicated in cancer etiology probably do not produce cancer by themselves but merely create the conditions for the manifestation and activation of latent tumor viruses already present in the host. The remaining 2/3 of the book is devoted to the immunological aspects of both transplanted and spontaneous tumors, with emphasis on the antigenic structure of malignant tissue and some of the newer techniques which have been used in this field. The possible relationships between the greater homogeneity of tumor tissues and the etiology of cancer are also pointed out, with special attention to the theory that cancer is due to a deficiency of protein or lipoprotein regulating factors controlling the reproduction of normal cells. Finally, some guidelines for future work are suggested and the principal outstanding questions are delineated. The book contains a wealth of experimental data and is thoroughly organized, with a subject index and a 2-part bibliography containing 280 Russian and approximately 810 Western references.

63-349 INTRODUCTION TO A DISCUSSION ON THE CANCER PROBLEM. (Fr.) de Stoppani, E. (Lugano, Switzerland). *Helv. Med. Acta* 29(5-6): 349-364, 1962.

Reviewed are the current concepts in the field of oncology, with particular attention to the incidence of cancer, the nature of malignancy and the etiology of neoplastic change. Data from the literature are presented on the cancer mortality by site and country, showing that the curve relating age and mortality in Switzerland is about the same for cancer as for mortality in general. The structure and behavior of the normal and malignant cell are contrasted schematically, and cancer is looked upon as a heritable cellular change produced by a variety of factors and leading to heterogeneous alterations in metabolism and growth. The possible causes of cancer are divided into endogenous factors (heredity and hormone balance) and exogenous stimuli including physical and chemical carcinogens, radiation and viruses. Finally, the various theories of carcinogenesis are reviewed and are tentatively synthesized into a general picture involving initiation by carcinogens, promotion by cocarcinogens, and the eventual development of clinical malignancy, all under the influence of many variables. (24 references)

63-350 THERE ARE NO "SENSATIONS"! (Ger.) Rudolf, W. (Innerkoflerstr. 36, Munich 5, Germany). *Ther. Gegenw.* 102(2):202-206, 1963.

After pointing out that the fundamental advances in science, such as the Watson-Crick structure for DNA, are seldom looked upon as sensational by the lay public, the author reviews the chronological development of the theory of the viral etiology of cancer, ending with the "sensational" finding by Levan and Nichols that common viruses such as measles have mutagenic properties which may well be responsible for malignant diseases such as childhood leukemia. Viruses currently recognized as carcinogens owe their carcinogenic potency largely to their chemical structure: those consisting of RNA nuclei (such as avian sarcoma-leukemia and mouse leukemia viruses) can induce tumors only when intact; while those rarer viruses which consist of DNA nuclei are oncogenic even as nucleic acid fragments ("infectious nucleic acids"). The mechanism of tumor initiation by the DNA group of viruses is thought to be, as with bacteriophage, through its effect on the genetic structure of the host cell. However, it must be concluded that RNA viruses also affect the genetic apparatus, not merely causing later aberrant growth through alteration of the cell surface. (No references)

63-351 RECENT DEVELOPMENTS IN THE VIROLOGY AND IMMUNOLOGY OF TUMORS. (Rus.) Abelev, G.I. and I. S. Irnin. *Vestn. Akad. Med. Nauk SSSR* 18(3):4-15, 1963.

At the sectional conferences of the VIIIth International Anticancer Congress in Moscow, 48 papers dealt with the role of viruses. According to L. A. Zil'ber, viruses act only as initiators of the neoplastic process and take no further part in the subsequent proliferation. American and Russian researchers presented recent findings on virus-induced animal tumors, and the possible role of these viruses in humans and their relationship to the common infectious viruses. New data presented confirmed the fact (first demonstrated in the USSR, Zil'ber et al.), that Rous sarcoma virus is pathogenic in several species of mammals (rats, rabbits, mice, guinea pigs, and hamsters). This oncogenic virus, like sheep pulmonary adenomatosis virus, has been found to produce cysts as well as tumors, thus indicating that certain types of pathogenic action are common to oncogenic and infectious viruses. Participants from the USA, England, and Israel gave new data on the virus agent recently discovered by Riley, et al. in various mouse tumors subjected to repeated transplantation; however, its etiologic role, if any, remains unclear. The problem of viral "parasites" in tumor cells was also discussed, as was the possibility of parasitization of solid cancers by leukemia viruses. Much material was presented on the pathology, epidemiology, morphology, and nucleic acid makeup of various leukemogenic viruses, some of them only recently discovered (10 identified to date), and other papers dealt with the isolation of oncogenic DNA. A number of contributions dealt with polyoma virus, including one on its ecology in urban and rural areas (Hubner); its possible etiologic role in human

disease remains to be determined. Wright reported on the epidemiology of human lymphoma in African children, and a special discussion was devoted to the viruses isolated from human leukemia and their immunologic properties. The many contributions to tumor immunology dealt with (1) the immunologic relationships between tumor and host and (2) studies on the antigen makeup of tumors. The data presented suggest that the specific antigens of carcinogen-induced tumors capable of inducing an immune response in the host are different even in tumors of the same site and origin, while those of virus-induced tumors are everywhere identical. Several papers dealt with experiments on immunization, with the problem of distinguishing immunity to viruses from immunity to tumor cells, and with the mechanism involved in the development of immunity to particular types of tumor, the role of isoantibodies in the "acceleration effect," etc. Revived interest in the possible clinical applications of specific anti-tumor immunization was reflected in the papers and discussions. A large number of papers dealt with the analysis of the antigen structure of tumors, and there were interesting and hopeful observations from the USA on the clinical uses--diagnostic and occasionally therapeutic--of labelled antifibrin antibody. Despite all the work done in the area of cancer immunology, none of the contributors has established the relationship of the observed changes in antigen structure, either to antitumor immunity or to the pathogenesis of tumors. Intensified research on autoantibodies may lead to a breakthrough in this area. (No references)

63-352 THE MECHANISMS OF ACTION OF CHEMICAL CARCINOGENS. (Rus.) Gel'shtein, V. I. Vestn. Akad. Med. Nauk SSSR 18(3):15-28, 1963.

At the VIIIth International Anticancer Congress in Moscow, among papers on chemical carcinogenesis, some of the topics covered was the relationship between chemical structure and carcinogenic potential, as revealed in the development and testing of new carcinogens (polycyclic hydrocarbons, oxy-compounds of noncyclic hydrocarbons, aminoazo compounds, nitrosamine derivatives, etc.), as well as older compounds. In analyzing the metabolism of carcinogens, 2 types of reaction were considered: detoxication mechanisms and the formation of carcinogenic intermediate products. While studies on the metabolic fate of carcinogenic compounds have been quite successful, the nature of the sensitive receptors is, as Haddow observed, less well understood; experimental data cited by this same author suggest the possibility that carcinogens may combine with nucleotides rather than with proteins. A number of papers dealt with the role of endogenous carcinogens, as demonstrated by tissue extracts and metabolic products from pts. with various types of cancer and leukemia. Other contributors discussed the carcinogenic action of chemically inert substances, of chronic irritation of the RES, etc. Several papers dealt with the interrelationships between viruses and chemical or physical agents, especially in the production of

leukemia. For example, a chemical carcinogen may act as the "initiator" of the neoplastic process, some other nonspecific factor acting as the "stimulator." In other cases, the initiator may be a virus or radiation, and a chemical agent (e.g., urethan) may act as the stimulator (Berenblum). Several contributors reported such phenomena as increased sensitivity to a chemical carcinogen (e.g., 20-methylcholanthrene) after viral infection (Duran-Reynals) or with hormonal stimulation (Haran-Ghera), reduced take of 9,10-dimethyl-1,2-benzanthracene (DMBA)-induced tumors in ovariectomized and adrenalectomized mice (Howell); and the significance of time factors in carcinogen-hormone interactions was noted by Symeonidis, Volfson, and others. Mody reported on the role of pseudopregnancy in mice in predisposing to the development of DMBA-induced ovarian tumors, and Dimant and Abdurasulova described the effects of removal of various endocrine glands on the incidence of DMBA-induced brain tumors in rats. The etiologic role of nutritional factors was discussed by Higginson; he concluded that kwashiorkor is the only nutritional disease that can be regarded as predisposing to hepatic cancer. The role of individual variation and genetic factors in susceptibility to cancer of the lungs and breast was analyzed by Heston, the genetic basis of predisposition to ovarian cancer by Murphy and Russell, and other contributors suggested the involvement of genetic factors in the differential susceptibility to 3,4-benzpyrene-induced skin and mammary cancers in mice (Bock), and in human hepatic cancer (Payet). Many papers were devoted to the analysis of the various stages of carcinogenesis, especially the initial changes and their specificity. A number of studies carried out with tritium-labeled precursors of DNA (thymidine) and RNA (uridine) indicated the value of this technic for studying the mechanism of carcinogenesis. Carcinogen-induced changes in the reactivity and morphology of precancerous and cancerous cells were described by several authors, while others discussed the possibility of some genetically based common factor underlying the induction of cancer by a great diversity of etiologic agents. (No references)

63-353 THE PROBLEM OF THE PRECANCEROUS STATE. (Rus.) Turusov, V. S. Vestn. Akad. Med. Nauk SSSR 18(3):81-86, 1963.

A special session of the VIIIth International Anticancer Congress was devoted to the precancerous stage. Neiman described the nonspecific nature of the initial changes, reflecting the nonspecific agents (physical, chemical, and biological) capable of causing prolonged minor tissue trauma, and Foulds discussed the factors responsible for their transformation into the definitely precancerous stage. Sirtori analyzed age changes in tissues and intracellular bodies predisposing to cancer development. Chiurco reported a large series of observations on occupational precancerous conditions and their initial reversibility. Clemmesen stressed the importance of collecting statistical data on precancerous states and

standardizing their nomenclature. Yoshida described the early stages of experimental carcinogenesis; a large number of papers dealt with the histology and histochemistry of precancerous conditions in individual organs. (No references)

- 63-354 THE PROBLEM OF THE LEUKEMOGENIC ACTION OF RADIATION. (Rus.) Tsessarskaia, I. P. (Cent. Inst. Hemat. and Blood Transfus., Moscow, SSSR). *Probl. Gemat.* 8(3):26-32, 1963.

In a review of the literature, the author poses the question of whether ionizing radiation acts directly on cells or affects them indirectly by first altering the humoral environment. Evidence for both mechanisms is cited from reports on the local, mutagenic, physicochemical, and biochemical effects of radiation. Although the problem is still far from being solved, the induction of mutations is regarded as the *sine qua non* of radiation-induced malignancy, and further elucidation of the decisive events at the cellular level is anticipated from studies on DNA metabolism, electron microscopy, histochemistry, and karyology. (92 references)

- 63-355 PRECANCEROUS LESIONS OF ENDOMETRIUM. (E.) Hertig, A. T. (Harvard Med. Sch., Boston) and H. Gore. *Zschr. Krebsforsch.* 63(3):201-208, 1963.

In this review of premalignant neoplasms, changes in the endometrial glands which precede adenocarcinoma, or are associated with its development, are studied in experimental and human material (autopsy, surgical specimens), supplemented by a study of pertinent case histories. Prolonged estrogen stimulation, unopposed by progesterone, may induce progressive histologic changes from simple hyperplasia and anaplasia (dysplasia) through carcinoma *in situ*, to invasive carcinoma, in pts. with ovarian granulosa-theca cell tumors. In one case illustrated, the successive stages developed over a period of 13-yr. In premenopausal pts. who are still ovulating, adenocarcinoma probably arises in an abnormal endometrial focus which fails to respond to progesterone. (14 references)

- 63-356 PREVENTIVE ASPECTS OF BRONCHIAL CARCINOMA. (Ger.) Heyden, S. (Dept. Prev. Med., U. Pennsylvania, Philadelphia). *Dtsch. Med. J.* 14(6):143-152, 1963.

An extensive review is presented of contemporary research on the etiology of lung cancer. Since adenocarcinoma and alveolar-cell carcinoma are not involved in the general increase in lung cancer, they are probably not caused by environmental factors; however, in squamous-cell carcinoma, cigarette smoking must be an important contributing factor in its increased incidence. The well known tobacco tar and skin cancer studies in experimental animals are reviewed, as are

postmortem studies in man showing a definite correlation between the number of cigarettes smoked and the severity of the progressive pathological changes in the bronchial mucosa, from basocellular hypertrophy to carcinoma *in situ*; *in vitro* studies have also shown that nicotine arrests ciliary movement, thus prolonging contact between the carcinogens and the basal membrane. Epidemiological studies have helped to clarify the relationship between bronchial carcinoma and variables such as cigarette and cigar consumption, air pollution (which is not believed to be an important etiological factor), predisposing diseases such as tuberculosis, chronic bronchitis, pulmonary emphysema, influenza, diabetes and others, and occupational exposure to carcinogens; it is pointed out that differences in smoking habits (inhaling, av. butt length, etc.) may help to explain the different distribution of lung cancer in various countries. Under preventive measures, the author disclaims the value of filter cigarettes and recommends discontinuation of smoking, since the pathological changes are generally reversible; health education of the youth is also urged, as well as systematic X-ray surveys of all smokers over 45, since the early symptoms are inconstant and unreliable. (83 references)

- 63-357 CARCINOGENIC SUBSTANCES IN MAN'S ENVIRONMENT AND METHODS FOR THEIR CONTROL. (Rus.) Shabad, L. M. (Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). *Vestn. Akad. Med. Nauk SSSR* 18(3):28-39, 1963.

A brief description is given of some of the more than 100 reports at the 8th International Cancer Congress devoted to the subject of carcinogenic agents. Reports were of 2 types: those dealing with the mechanism of action of carcinogens and theories of carcinogenesis, and those dealing with environmental carcinogens and ways in which their effects on man can be decreased. In conclusion, the author emphasizes the broad range of subject matter covered in these reports, the wealth of valuable factual information presented, and the many suggestions, both for improving the quality of research and for more effective preventive public health measures. (No references)

- 63-358 CANCER IN FLAX SPINNERS AND ITS SIGNIFICANCE FOR CANCER RESEARCH. (Ger.) Körbler, J. (Oncol. Inst., Zagreb, Yugoslavia). *Beitr. Krebsforsch.* 8:1-108, 1962.

On the basis of a detailed review of the literature and a report of 30 years of personal research, the author concludes that flax contains carcinogenic substances which are implicated in the etiology of cancer of the lip. Among 187 women with cancer of the upper lip (age range 27-84, mean survival 59.33 yr.), the average time interval between the beginning of spinning and the appearance of the disease was: in 13 who used only or mostly flax, 47.6 yr.; in 7 who used

predominantly hemp, 47 yrs. Among 192 women with lower lip cancer (age range 26-84, mean survival 60.45 yr.), in 39 who used mostly or only flax, interval was 49.58 yr.; in 25 who used predominantly hemp, 48.18 yr.; in 5 who used wool, 33.8 yr. The latent period was longer in those women who began to spin at an early age. Histologically all tumors were carcinomas. The cancer formation was preceded by a more or less chronic inflammation; in lower lip cancer early removal from the carcinogenic environment could lead to regression (2 cases were presented). While the author believes that simple mechanical irritation can cause cancer (1 case history is presented), he also thinks that this is not the cause of lip cancer in spinners. Pulverized flax threads (suspension in Ringer's solution, 1 ml, s.c.) in mice induced carcinoma in 3/100, and leukemia in 5/100; carcinoma was found in 1/30 that received a similar suspension but in saliva, and in 2/10 that received an extract from the smoke of burned flax threads; leukemia appeared in 1/35 mice given s.c. an alcohol extract of a flax thread suspension in Ringer's solution; an alcohol extract suspended in saliva was ineffective. Pulverized cigarette paper suspension in Ringer's solution after s.c. admin. produced leukemia in 1/22 mice; when small pieces were implanted into the skin, 1/10 mice developed carcinoma and 2/10 leukemia; an extract from cigarette smoke, ash or pulverized material suspended in saliva did not produce lesions. The induced tumors were transplantable; tumors of the third transplant generation showed pronounced infiltrative growth. In mice with leukemia induced by injection of flax fiber suspension, the shortest latent period was after 3 injections and the longest, after 1. Blood from leukemic mice produced secondary leukemia in 13/23 mice when injected i.v. (but not i.p.); incubation time was 1-6 mo. Blood supernatant, given i.v., produced secondary leukemia in 1/5 mice (blood centrifugate and frozen blood did not). Topical application of various aqueous extracts of cigarette paper smoke, after 5 mo. induced leukemia in 5/13 mice; an alcohol extract was ineffective. Topical application of aqueous or alcohol extracts of tobacco smoke alone did not induce leukemia or carcinoma. In view of the production of such a variety of transmissible neoplasms, the possibility of a viral etiology is suggested, and a general theory of carcinogenesis is propounded which unifies all types of malignancy as the variable expression of essentially the same irritative stimuli. In support of this concept, extensive work is also reported on the transplantation of animal tumors, the transmission of mouse leukemia to rats, and the nature of carcinosarcoma. The direct inheritance of mouse leukemia is also discussed. Precancerosis in flax-workers is also discussed: 8/11 male workers (age 16-33 yr., working period 2-5 yr.) and all 10 female workers (age 17-51 yr., working period 1-5 yr.) showed more or less pronounced hyperkeratosis on the dorsal surface of the hands. Chemical composition of the flax-fiber is reviewed from the literature. The paper chromato-

graphs of the extracts of cigarette paper, flax-fiber and pipe sediment showed bluish fluorescence at the same spot; these fluorescent spots are not 3,4-benzpyrene or 20-methylcholanthrene or their simple derivatives or anthracene. Finally, some of the work on carcinogenic plastics and on cancer in the cotton spinning industry is reviewed. (299 references)

- 63-359 SKIN AS A TEST SITE FOR THE BIOASSAY OF CARCINOGENS AND CARCINOGEN PRECURSORS. (E.) Poel, W. E. (Grad. Sch. Public Health, U. Pittsburgh, Pa.). *Nat. Cancer Inst. Monogr.* (10):611-631, 1963.

This discussion revolves chiefly about the author's own studies. 3,4-Benzpyrene (BP; 0.002%-1.25% in toluene, 0.0075 ml) was applied by measured drop to the shaved interscapular skin of SWR, C3HeB, and A/He male mice 3 x/week until death or persistent skin tumor formation. At 0.38 µg of BP, 2/22 SWR and 3/17 C3HeB mice formed benign tumors 55 week and 81-93 week, resp., after first exposure; at 0.75 µg, 15/18 SWR mice formed malignant keratinizing tumors (25-72 weeks) and 4/17 C3HeB formed benign tumors in 51-93 weeks. At 19.0 µg, 54/56 mice of all three strains formed malignant tumors and with a shorter latent period. At a dose of 470 µg all mice formed malignancies in 4-21 weeks. The thresholds for any tumor induction by a topical carcinogen for premalignant tumors, for malignant tumors, and the time required for their induction, all varied with the strain used, but in all, high concentrations reduced life span. For bioassay of carcinogens, using skin, the most susceptible and hardy strains are desirable. A summation of neoplastic response was obtained to sequential exposures of mice to a strong and a weak carcinogen; hence, for a more sensitive bioassay of skin carcinogenicity, pretreatment with local applications of a standardized, potent carcinogen is suggested. After gastric intubation of SWR mice with 20-methylcholanthrene (MCA; 1.0 or 0.25%, 0.1 ml) in Tween 60 2 x/week for life, 17/37 developed skin carcinomas in 14-34 weeks, but controls and mice treated with BP alone developed none. Similar admin. of 9,10-dimethyl-1,2-benzanthracene (3 mg x 2/week for 1, 2, or more weeks) in Tween 60 to C57Bl/6 mice proved highly toxic after 3 doses, but it did induce benign skin tumors in 10/32 mice intubated twice with 3 mg. A proposed classification of carcinogens divides them into topical carcinogens (including those either resistant or prone to metabolic degradation), carcinogen precursors (agents whose conversion to a potent state depends upon the metabolism of the host), and hormonal supplements, inhibitors or antimetabolites. To conform with the characteristics of each of these three types of carcinogens, two-stage sequential technics of bioassay are proposed. (17 references)

- 63-360 THE MECHANISM OF ACTION OF CARCINOGENIC FACTORS. (Ger.) Dannenberg, H.

(Max-Planck-Inst. Biochem., Munich, Germany).
Deutsch. Med. Wschr. 88(13):605-616, 1963.

After pointing out that the mutational theory of carcinogenesis requires a direct relationship between the various factors known to produce cancer (organic compounds such as polycyclic aromatic hydrocarbons, aromatic amines or alkylating agents; inorganic compounds; physical factors such as UV light and ionizing radiation; and tumor viruses) and the hereditary components of the cell, the author reviews the chemical structure and role of the nucleic acids as carriers of the genetic code. The Watson-Crick structure of DNA and the role of regulator, operator and structural genes in specific protein synthesis are described in detail. It is pointed out that tumor viruses may contribute new DNA and hence new genetic information to the infected cell, while other carcinogenic agents must alter the structure of the native DNA molecule. The spatial resemblance between aromatic carcinogens and the base pairs in double stranded nucleic acids is pointed out and the entry of the carcinogen molecule into the DNA strand is hypothesized; this would, however, require prior expansion of the compact DNA molecule. Finally, a distinction is made between active and inactive genes, and hence between active and inactive DNA, and it is suggested that it is precisely the most active DNA which exists in the loosest structure (the "puffs" at active sites of the chromosomes), facilitating the entry of chemical carcinogens. On the basis of insect metamorphosis and the incidence of mammary tumors in rats of various ages, the hormonal activation of genes is postulated. (71 references)

63-361 THE ETIOLOGY OF DISEASE, WITH SPECIAL REFERENCE TO RHEUMATOID ARTHRITIS, MULTIPLE SCLEROSIS AND CARCINOMA (ON THE BASIS OF FINDINGS IN THE EYE AND THE SKIN). (Ger.)
 Passow, A. (Julius-Maximilians U., Würzburg, Germany). Zschr. Ges. Inn. Med. 17(24):1096-1104, 1962.

After discussing the role of metabolic disturbances in the development of generalized dystrophic, exudative and necrotic phenomena such as in rheumatoid arthritis, multiple sclerosis and retrobulbar neuritis, the author draws a parallel between these visible results of intoxication and the appearance of carcinoma. He emphasizes that the same chemical and physical factors which at high doses, produce cellular intoxication and lead eventually to diseases such as multiple sclerosis, may, at low doses, lead to uncontrolled, possibly compensatory, cellular proliferation and eventual malignant degeneration. Thus, chemicals such as As, tars, H₂S, CS₂, hydrocarbons, CO, nitrobenzene, aniline dyes, tobacco and alcohol as well as thermal burns or irradiation, may lead to either retrobulbar neuritis, due to damage to the maculopapular fibers of the optic nerve, or carcinoma depending on constitutional factors and the intervention of the autonomic nervous

system. The basic lesion in carcinogenesis by either exogenous or endogenous carcinogens would seem to be mitochondrial damage leading to excess glycolysis and an irreversible, functional disturbance in protein and hence enzyme synthesis; during this stage, corresponding to precancer and perhaps lasting several decades, nuclear mutations are produced and the cell responds by uncontrolled proliferation, leading eventually to metastasis and general intoxication. (62 references)

63-362 THE EPIDEMIOLOGY OF CANCER. (Rus.)
 Chaklin, A. V. Vopr. Onkol. 9(1): 13-19, 1963.

The author briefly reviews some of the papers in the field of cancer epidemiology presented at the VIIIth International Anticancer Congress in Moscow in the summer of 1962. (No references)

63-363 TOBACCO SMOKING AND DISEASE. (E.)
 Lowe, C. R. Curr. Med. Drugs 2(4): 18-23, 1961.

Briefly reviewed is the literature on the statistical, pathological and experimental evidence for the association between smoking and lung cancer; also discussed are the constitutional factors which may predispose people to both smoking and lung cancer and therefore produce the statistical coincidences so often cited. Evidence for a relationship between smoking and chronic bronchitis, tuberculosis, hypertension, coronary artery disease, peptic ulcer, premature births, industrial absenteeism and accidents, and cancer of the bladder is dealt with briefly. (35 references)

63-364 REMISSION IN LEUKEMIA. (Sp.)
 Mas y Magro, F. (Plaza Calvo Sotelo, 12, Alicante, Spain). Arch. Med. Exp. (Madrid) 24(1):55-64, 1961.

The author is convinced that human leukemia is a disease of viral etiology; that there are probably persons who are resistant to it, as in the case of other virus infections; that it regresses spontaneously in the "cryptoleukemic" stage in 90% of those affected, without ever being diagnosed; and that it progresses to the frankly leukemic and fatal stage only in particularly labile organisms or where some intercurrent viral infection supervenes—in the latter case through the "viral interference phenomenon". In acute leukemia, the triggering factor is usually a viral infection, although some cases may be induced by chemical agents or, in an organism already attacked by a latent virus infection, by trauma. The more numerous and more prolonged remissions now being achieved in leukemia suggest that the disease is potentially "treatable"—initially, at least, and that it may not be the actual viral agent which dictates a fatal outcome, but some other intervening factor, e.g., exhaustion or breaching of the organism's defenses by the metaplasia itself. (19 references)

- 63-365 REPORT OF THE CONFERENCE OF THE HUNGARIAN BOARD OF SCIENTIFIC ADVISORS ON PUBLIC HEALTH CONCERNING PRECANCEROUS TUMORS. (Ger.) *Neoplasma* (Bratisl.) 9(6):597-623, 1962.

T. Venkei reviewed the various concepts and observations on precancerous states and classified them as facultative precancerous (1) in the broader sense, i.e., basic diseases such as skin changes due to X-rays, radium, radioactive isotopes, arsenic, tar and its derivatives, etc.; in less than 6% of which squamous epithelial cancer is found, or (2) in a narrower sense, keratoprecancerous lesions, more than 10% of which become cancerous (as in 32/276 of the author's cases of keratoma senile, 7/64 of cornu cutaneum, 23/152 of keratoacanthoma, and 19/168 of leukoplakia). The other group, obligatory precancerous, includes such conditions as xeroderma pigmentosum and the preinvasive cancers in Bowen's, Queyrat's and Paget's disease, which sooner or later all become cancerous. The relation of the treatment to the nature of the lesion as well as malignant changes in pigmented nevi are discussed. J. Sugár described in detail the histologic changes seen in various precancerous dermatologic conditions in relation to the preceding classification. L. Váczy and B. Kellner gave similar descriptions for uterine and mammary tumors, resp. F. Prochnow said that mastopathies could not be considered invariable precursors of mammary cancer and urged greater reliance on histologic rather than on clinical findings. E. Hedri stated that the incidence of subsequent cancer was 3-10% for simple hyperplasia; 20-30% for demonstrably precancerous hyperplasia; 2-4% in the presence of atypical cytologic structure; and none in the presence of fibrosis or fibroadenosis. B. Korpássy accused the pathologist of isolating himself behind a "paraffin curtain", questioning the possibility of anticipating subsequent cancerous changes by histomorphological studies. He pointed out that atypical, cancer-like epithelial proliferation was common in the bronchi of infants with measles and that spontaneously reversing changes resembling carcinoma were also seen in the portio uteri during pregnancy. M. Melczer said that measurement of resistance to polarization (the Melczer-Kiss electrometric technic) had been successful in distinguishing premalignant from malignant cutaneous cancers and melanoblastomas; and that studies will now be extended to suspected uterine and buccal carcinomas, although this technic is not being considered for the study of mammary cancers. L. Kuti commented on reports that 2-3% of all mastopathies became cancerous and said that his experience indicated a much higher percentage. B. Kellner summarized the findings of the conference, pointing out that the greatest disagreement was over the prognostic implications of cystic mastopathies; he also stressed the need for simplification of colposcopic nomenclature. (No references)

- 63-366 THE CARCINOGENIC ACTIVITY OF IONIZING RADIATION. (Rus.) Sviatukhin, M. V. *Vestn. Akad. Nauk SSSR* 18(3):39-43, 1963.

Brief summaries are given of the contents of 29 papers read in the Radiology section of the VIIIth International Anticancer Congress in Moscow, dealing with the effect of various types of ionizing radiation in the promotion of cancer, their effect on the growth of established tumors, their side effects, and the prevention of harmful complications. Several authors discussed the genetic factors in tumor induction by radiation. (No references)

- 63-367 EVALUATION OF CARCINOGENICITY. (Fr.) Gillon, J.-J. *Concours Med.* 85(15): 2325-2326, 1963.

An editorial provoked by the recent issue of a report by the WHO on carcinogens in food additives. The importance of a protocol which will allow "scientific" interpretation of results is stressed. However, integration of experimental results, no matter how carefully obtained, with human carcinogenesis involves a number of pitfalls. The author emphasizes our lack of knowledge of the effects of summation of drugs in animals as well as in man. (No references)

- 63-368 THE EPIDEMIOLOGY OF CANCER. (Rus.) Sviatukhina, O. V. *Vestn. Akad. Med. Nauk SSSR* 18(3):76-80, 1963.

Thirty papers were devoted to this relatively new trend at the VIIIth International Anticancer Congress in Moscow. After discussing the applicability of the term "epidemiology" to cancer research and the statistical methodology appropriate to its investigation, the author gives brief summaries of the papers presented. Most of the contributors reported the incidence of particular forms of cancer in different countries and attempted to relate these findings to environmental factors. Thus betel nut chewing was correlated with the large proportion of oral cancers in India; dietary factors and cirrhosis with cancer of the liver among the aborigines of Australian New Guinea; opium smoking with nasopharyngeal and esophageal cancer among the Chinese of Singapore; virus-carrying mosquitoes with the high frequency of malignant lymphoma (reticulosarcoma) in a particular area of tropical Africa; etc. Other factors discussed included the relationship between circumcision and cancer of the cervix in the wife and the role of exposure to sunlight in skin cancer. The various prophylactic measures suggested by these findings are discussed.

- 63-369 THE MECHANISM OF CELL REPRODUCTION AND CARCINOGENESIS. (Rus.) Tuniaikov, G. G.

(Moscow Techn. Inst., Meat and Dairy Indust.) and
Iu. G. Tuniakov. Ark. Pat. 25(3):9-26, 1963.

On the basis of their own experiments and data in the literature, the authors present their concepts of precancerous proliferation, nuclear aberrations, and ultimate malignant change. In the examination of over 50,000,000 cells (from 45 normal, benign and malignant tumors from man and animals), the index of mitotic activity and the frequency of genome variability (reorganization of the nucleus as a whole) and chromosome variability (modification of individual chromosomes) were used as the criteria for comparing various groups of tissue. For normal tissues showing little proliferation, the mitotic index (MI) was low (0.02-0.12%), only 3.2% of the cells showed chromosome reorganization (anaphasic bridges); there were no genome aberrations. In vigorously proliferating normal tissues, the MI was 0.5%, with significant genome and chromosome variability (28% in spleen and 30% in embryonic tissue, 50% or more in bone marrow). In benign tumors (6 types of fibroma), the mitotic index was very low (av. 0.038%), with less disturbance of anaphase (0.5%) than in controls, and greatly heightened fiber forming activity, reflected in hypertrophied fibroblast nuclei. In precancerous tissues (2 rectal polyps and one human inguinal papilloma), the MI was relatively high (0.58%), with a great increase in the number of anaphases showing chromosome reorganization (28.6%) and in the over-all index of chromosome variability (almost 43%), and genome reorganization in the form of tri- and multipolar anaphases. In all of the malignant tumors (13 human and 10 animal carcinomas and sarcomas), the MI was near or above 1%, with a high frequency of chromosome abnormalities (60-83% anaphases showing bridges and fragmentation) and a significantly greater number of cells showing genome reorganization (11% metaphases with chromosomes at poles and 4.2% tripolar anaphases). Whatever the factors or causes conducing to cancer may be, they all share the capacity for evoking the natural mechanisms of nuclear variability, while all malignant tumors are quantitatively different in the way the various dicentric chromosomes break and in the number of dissimilar population lines of malignant cell present in each. (79 references)

63-370 EFFECTS OF DIAGNOSTIC IRRADIATION.
(E.) Rabinowitch, J. Lancet
1963, 1963.

In a letter to the editor, the writer (a radiologist) advocates the resumption of prenatal radiologic pelvimetry, on the ground that this procedure can save many thousands of lives annually at birth, as against a very few (20-30) leukemic deaths which might be due to diagnostic radiation. He also suggests that respiratory infections that are often associated with the pre-leukemic state, may be the cause (or trigger) of leukemia, rather than diagnostic X-rays. (no references)

63-371 HUMAN CANCER: MENDELIAN INHERITANCE
OR VERTICAL TRANSMISSION? (E.)

Burch, P. R. J. (Dept. Med. Phys., U. Leeds, England). Nature (London) 197:1042-1045, 1963.

In a theoretical discussion of the familial incidence of leukemia and other neoplastic diseases, the author reviews some of the evidence indicating that Gross' theory of the direct transmission of an oncogenic agent (i.e. virus) from parent to child is, at best, superfluous. In previously published discussions, the author deduced that malignancies in adult human beings generally develop from cells containing 4 specific (nuclear) gene mutations (2 on each of 2 homologous genes), 1 of which is often inherited, the remainder originating in 1 or more somatic cell lines. The incomplete penetrance of the inherited mutation is due to the low probability that a somatic cell will acquire the 4th carcinogenic mutation within the normal life span. In children, however, an additional, nongenetic stress factor such as hormonal stimuli, pyogenic infections or horizontally transmitted oncogenic viruses must be operative. Evidence presented includes the fact that the frequency of childhood leukemia in multiple siblings can be approximately accounted for by calculating both the size of genetic carrier subpopulations and the penetrance of an inherited mutation, assuming a reasonable mutation frequency at 2 or more leukemogenic loci; besides, the inheritance factor in leukemia can be demonstrated cytogenetically, the most prevalent site of involvement being chromosome pair 21. Leukemic pedigree evidence showing that transmission from the father is just as common as from the mother also supports the genetic theory. Finally, cancer mortality trends (a steady incidence rate of pre-zygotic cancers over the yr.) and twin studies (9.8% concordance in monozygotic twins compared to 5.1% concordance in dizygotic) are cited. Some of the discrepancies between statistical surveys in different areas are explained by the fact that the increased susceptibility of adult, leukemic, genetic carriers to infectious and parasitic diseases results in an inverse correlation between mortality from leukemia and that from infection, and a decreased ratio of pre-zygotic to post-zygotic leukemias in areas with high mortality from infections. (43 references)

63-372 CARCINOGENESIS AND CANCER PREVENTION.
(E.) Burch, P. R. J. (Dept. Med. Phys.,
U. Leeds, England). Nature (London) 197:
1145-1151, 1963.

Before presenting a theoretical treatment of the roles of gene mutations, viruses, hormones and immune reactions in malignant transformation, the author points out that even though most human malignancies are probably genetic in origin (see preceding abstract) and the involvement of viruses, at least in adult cancer, is probably rare, eugenic practices could still decrease the incidence of

pre-zygotic cancers, while that of post-zygotic cancers may be reduced in various ways. The process of carcinogenesis is divided into the initiation stage (random accumulation of mutant nuclear genes or gross chromosomal defects in a generative somatic cell), the carcinogenic nucleotype (involving 4 specific mutations at the regulator and operator-structural loci on homologous genes), the carcinogenic cell (in which the cytoplasmic constitution reflects the nuclear changes), the latent period or promotion stage, the premalignant cell (which may have only 3 of the 4 mutations) and the cancer cell; the mutant genes may be inherited or induced by radiation or viruses, and viruses may also affect the latent period. On the basis of the characteristics of the latent period and the replacement of differentiation by duplicating mitosis in neoplastic tissue, a hypothesis is suggested according to which the mutant structural gene produces mutant RNA which results in the synthesis of a lipoprotein with an abnormal amino acid sequence which will be autoantigenic. An immune reaction between this autoantigenic lipoprotein and appropriate antibody at the endoplasmic reticulum affects the nature of differentiation-mitosis metabolites in the cytoplasm. Normally, the presence of a differentiating factor (DF) and repressor molecules from non-mutant regulator loci produce a pattern of inhibition and release of structural loci appropriate to ordinary differentiation. However, in the presence of mutant regulator genes, the lack of DF or presence of abnormal DF (NDF) causes the mutant repressor plus NDF to inhibit mutant RNA synthesis at the mutant structural locus. The concentration of autoantigenic lipoprotein is therefore reduced and the source of DF is irreversibly diminished; at this point, normal differentiation is no longer possible, even in the absence of antibody, and the pattern of structural locus activity is that of a malignant cell. Premalignant hyperplastic transformation is accounted for by cells containing only 3 mutations (1 at the structural locus and both regulator loci). Similarly, hormones with mitotic-stimulating properties may yield hormone dependent neoplasms in which the cells have homozygous mutant-regulator genes and heterozygous mutant-structural genes; a 4th mutation would then permit autonomous growth. The implications of this theory for the inheritance of cancer susceptibility are discussed. With respect to oncogenic viruses, several etiological roles are possible within the framework of the mutation hypothesis: they may act as a cocarcinogen; virus proliferation may affect the synthesis of DF, control lipoprotein or mutant RNA; a DNA virus might transduce or mutate a regulator gene or affect it by a lysogenic type action, or similar effects might be exerted on operator-structural control genes. Although cancer cells have thus both lost and acquired specific antigens, autoantigens are present in only very low concentrations so that conventional immunization is unlikely to succeed. The opposite procedure, represented by the induction

of acquired immune tolerance or immunological paralysis, may result in dormant cancer cells which would not develop beyond the latent period. This requires the identification and isolation of cancer-specific antigens and their continuous admin., in high concentrations, during embryonic development. Finally, the possibility that the elimination of cancer could result in the accumulation of mutant, otherwise carcinogenic, genes in the population, which might have other detrimental effects, is considered. (55 references)

- 63-373 ETIOLOGY AND DEVELOPMENT OF CANCERS. (Ger.) Schmähl, D. (Inst. Path., Rheinische Friedrich-Wilhelms U., Bonn, Germany), and W. Krischke. *Internist (Berlin)* 4(3):71-76, 1963.

Supplementing a general review of the literature (including some of his own previously published work), the author discusses the virus theory of carcinogenesis, the presumed mechanisms of action of exogenous carcinogens, theoretical changes taking place in the transformation of a normal into a malignant cell, and the known mechanisms of action involved in metastasis. He concludes that a viral etiology has yet to be demonstrated for cancers occurring in man; and that metastasis is at least partially conditioned by constitutional defense mechanisms: not only in a general, overall sense, but in terms of a wide variation in the strength of such defense mechanisms as between organ and organ or between other potential sites of tumor development. (33 references)

- 63-374 SPECIFIC ETIOLOGIC FACTORS IN CUTANEOUS CANCERS. (Sp.) Degos, R. (Fac. Med., U. Paris Sorbonne, France). *Actas Dermosif.* 53(6):303-322, 1962.

A general review of factors which may favor the development of cutaneous cancers includes discussion of the roles of accidental trauma, repeated (minimal) trauma, chemically-induced trauma, UV, other forms of radiation, cutaneous scarring, specific carcinogens (chiefly industrial), and chronic inflammatory dermatoses. (No references)

- 63-375 A MEASURABLE CONSTITUTIONAL DEFENSE MECHANISM EMPLOYED BY THE BODY AGAINST THE DEVELOPMENT OF MALIGNANT TUMORS. (Dut.) Audier, A. G. (Lab. Trop. Hyg., Leiden, The Netherlands). *Acta Leidensia* 32:20-31, 1963.

Within the framework of a general discussion on the various factors involved in susceptibility to cancer, including inheritance, prenatal effects and environmental exposure to carcinogens and anticarcinogens (infections, allergies, bee venom, epilepsy), the author analyzes the elements predisposing to tumor development, with particular emphasis on the role of the nervous system, and reports some preliminary experiments

In man and animals. It is pointed out that attempts have been made to relate the incidence and malignancy of tumors to body build, physiological and psychological characteristics and/or psychoanalytic factors. In Pavlovian terms, more tumors have been said to develop in animals with the "strong unequilibrated" type of central nervous system than in those with "weak" nervous systems. He also reviews the changes in the bodily defense mechanisms which may result from adaptive changes or metabolic deficiencies induced by tumor growth and notes reports in the literature indicating that the plasmin level in the blood increases in the presence of malignancy. In experiments on rabbits inoc. intratesticularly with Brown-Pearce tumors, admin. of pilocarpine (which consistently increases the blood plasmin level), had no effect on tumor growth; but a strong correlation was seen between rapid recovery from the effects of pilocarpine and resistance to tumor development. The 4/11 rabbits in which no tumors developed within 2 weeks (or later) were those in which the plasmin level returned to normal or below normal most rapidly. Similarly, the plasmin level returned to normal within 3 hr. after inj. of bacterial polysaccharide in 25/47 inoperable cancer pt.; 1 mo. later, 20 of these 25 were still alive, compared to none of the other 22. On the basis of the literature and these preliminary experiments, the author concludes that the speed of recovery of the blood plasmin level after exposure to stress may be a useful measure of the defensive capabilities of the organism. (54 references)

3-376 CARCINOGEN-INDUCED MELANOTIC TUMORS IN ANIMALS. (E.) Nakai, T. (Div. Oncol., Chicago Med. Sch.) and H. Rappaport. Int. Cancer Inst. Monogr. (10):297-322, 1963.

A detailed review of previously published work on the morphology and histology of the multiple melanotic tumors produced in the Syrian hamster, golden or white, by either a single topical application of 9,10-dimethyl-1,2-benzanthracene (1% in mineral oil) or p.o. or p. admin. of urethan, the authors emphasize that these benign tumors, which rarely metastasize, are limited to the dermis with no involvement of the epidermal junction, being composed of dermal melanocytes and resembling the cellular blue nevi or pigmented neurofibromas in man; in contrast, malignant melanomas, which occur rarely and only in the golden hamster, do involve the epidermis and frequently metastasize. The tumors are derived from nonpigmented dermal melanocytes or those with nascent pigment granules, which are susceptible to the action of the carcinogen, while the pigmented melanocytes and all epidermal melanocytes are resistant. The resistance of the epidermal melanocyte may so explain the rarity of spontaneous malignant melanoma in this animal. The fine structure of the pigment granules in the developing melanotic

tumors is described in detail, and differences between the white and golden hamster are pointed out. Detection of neural elements in these tumors supports the hypothesis that the tumor cells are of endoneural and probably Schwannian origin, the primary source probably being cells of the neuroectodermal mesenchyme of small dermal nerves. (34 references)

63-377 FURTHER REVIEW OF REPORTS ON THE LATE EFFECTS OF THE ATOMIC BOMBING OF HIROSHIMA AND NAGASAKI. (Cz.) Akimoto, S. (New Jap. Doctors Assoc., Hiroshima, Japan), K. Honda, N. Kusano, H. Nakamura and H. Shiga. Cesk. Zdrav. 10(9):466-479, 1962.

A review of data published after 1957 showed that the death rates due to radiation exposure were still above normal; that incidence of leukemia showed possibly a decreasing trend after 1960; that incidence of lung, stomach, thyroid, and genitourinary neoplasms was still increased; that incidence of anemia and leukopenia was still increased among the exposed; that the residual radiation and/or late effects still resulted in new cases of radiation sickness; and that the weakness and malaise syndrome is still very common. (12 references)

63-378 CARCINOGENIC EFFECT OF PETROLEUM AND ITS BY-PRODUCTS. (Rus.) Gimadeev, M. M. Kazan. Med. Zh. 2:79-84, 1962.

A review of literature on the carcinogenic effect of petroleum and its by-products are briefly discussed. Many of the products can induce hyperkeratosis, folliculitis, verruca, pulmonary adenoma, skin cancer, etc. Their action is mainly local but they can also be multicentric. Although a number of groups have made chemical analyses of various petroleum and petroleum products, results were generally negative with respect to 3,4-benzopyrene, although 40-68 µg/g was found in 1 crude petroleum. At present it appears that much of the carcinogenic action of these materials resides in polycyclic hydrocarbons about which little is known. (72 references)

63-379 ERYTHROCYTE ADSORPTION METHOD IN THE STUDY OF CARCINOGENIC VIRUSES AND SPECIFIC TUMOR ANTIGENS. (Rus.) Liubogovskaia, L. A. (Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR, Moscow) and L. V. Shershul'skaia. Vop. Onkol. 9(2):118-126, 1963.

A review of literature on the elution and adsorption of carcinogenic viruses (Rous, Shope, polyoma), adsorption of tumor nonspecific animal antigens of serum and tissue extracts, and of specific antigens of human neoplasms by RBC's was presented. Polyoma virus has the ability to agglutinate RBC; it is most sensitive to those of the frog and guinea pig. Also chick RBC, after

contact with rat hepatoma, can be agglutinated with the serum of these animals; Brown-Pearce and M-1 tumors had less effect. Guérin tumors, sarcomas 16 and 380, and fibrosarcoma 45 gave negative results. Rabbit RBC, treated with extracts from human tumors, were agglutinated by serum of these pts. Antigen differences were demonstrated between normal and tumor (leukemic) RBC. Yet the nature of the specific antigens of human tumors, and the mechanism of interaction between the filtrates extract and RBC remains as yet not clear. The adsorption method was useful in identifying the properties of some carcinogenic viruses, in studies on the structure of Shope's papilloma antigen, and in the isolation of purified polyoma viruses. (88 references)

63-380 CUTANEOUS PRECANCEROUS CONDITIONS IN MAN. (E.) Graham, J. H. (Skin and Cancer Hosp., Philadelphia) and E. B. Helwig. Nat. Cancer Inst. Monogr. (10):323-333, 1963.

In this extensive report and review is discussed the incidence, pathology and clinical development of the precancerous dermatoses and particularly their relationship to cutaneous and internal cancer. Among 155 pts. (212 lesions) with Bowen's disease (av. age at onset 48.4 yr.), Caucasian males with combinations of light complexion, hair and eyes, who had spent most of their lives in the southern United States, predominated. A total of 238 premalignant and malignant lesions of the skin (senile keratosis, basal cell carcinoma, squamous carcinoma, adenoacanthoma, melanoma, etc.) were seen in 64 pts., and 25% had primary internal or extra-cutaneous cancers. A total of 75 pts. (48.4%) had premalignant lesions and/or primary cancer in 1 or more locations, appearing an av. of 5-7 yr. after the onset of Bowen's disease. A similar incidence of premalignant lesions and/or primary cancer (66%) was previously reported in 15 pts. with arsenical keratosis, the lesions being clinically and histologically practically indistinguishable from those of Bowen's disease. A significantly greater proportion of pts. with either Bowen's disease or arsenical keratosis had high arsenic levels in the lesions and adjacent skin. The natural history of 50 pts. with Queyrat's erythroplasia of the glans penis (median age 52 yr., 43/50 Caucasian; internal cancer in 2/50 and cutaneous premalignant lesions of senile keratosis or basal cell carcinoma in 3/50; invasion of the underlying stroma in 7/50 and distant metastasis in 2/7) indicated that this is a different disease entity than Bowen's disease. Among 144 pts. (216 lesions) with senile keratosis (predominantly Caucasian males with an av. age of 62 yr.), 18 showed 26 lesions with histologic evidence of invasion of the corium; none were metastatic. Above-normal levels of arsenic were seen in 10/17 lesions. A study of 40 pts. with Paget's disease of the anogenital region revealed an associated adnexal skin cancer or primary cancer of the rectum, urethra or breast in at least half of the pts. (predominantly

Caucasian females, median age at onset 59 yr.). This high incidence of associated cancer probably results from the multicentric effect of an unknown carcinogenic stimulus. Finally, preliminary observations on 76 pts. (predominantly Caucasian males, median age 50 yr.) with Jadassohn's intraepidermal epithelioma showed that this condition, which may be confused histologically with Bowen's disease except for lower arsenic levels, is not associated with high internal cancer incidence: among 76 pts., 3 had internal cancer, 10 had cutaneous premalignant lesions of senile keratosis, squamous cell carcinoma, malignant melanoma and/or basal cell carcinoma. However, 6/76 showed microscopic evidence of local invasion of the corium and 1/6 had regional metastasis, indicating that this is also a precancerous dermatosis. (14 references)

63-381 ELIMINATING THE CARCINOGENIC PROPERTIES FROM THE PRODUCTS OF THE PROCESSING OF OIL SHALES. (Rus.) Bogovskii, P. A. (Inst. Exp. Clin. Med., Estonian Acad. Sci.). Vestn. Akad. Nauk SSSR (8):72-75, 1962.

In a general review of recent work the author points out that the carcinogenic activity of products derived from oil shales is generally proportional to the temperature of preparation of the resin, its specific gravity and the content of 3,4-benzpyrene. Thus, the most carcinogenic are the high-temperature chamber resins, followed by tunnel resin and generator resin, while the neutralized generator resin used as a plasticizer in the rubber industry and the shale drying-oil used in typographers ink are non-carcinogenic. However, chromatographic studies of chamber resin have revealed fractions which are still carcinogenic although they contain no 3,4-benzpyrene, as well as other components which can either promote or antagonize the action of 3,4-benzpyrene. A benzene extract of the soot formed during the roasting of shale has also been found to be highly carcinogenic. The benign and malignant tumors produced by application of these resins to the skin of white mice include characteristic, extremely dedifferentiated epidermal cancers which are indistinguishable from spindle cell sarcomas ("cytoblastomas"), and benign proliferations of the subepidermal adipose tissue ("mastocytomas"). Finally, the carcinogenic activity of resins can be altered by treatment; e.g. the carcinogenicity of chamber resin can be increased by removal of phenol, or decreased by blowing air through the material. The best way of decreasing the carcinogenicity is by coking, i.e. use of the distillate after distillation at atmospheric pressure or above. Treatment of resins with high-frequency currents or ultrasonic radiation is also effective, but the best ultimate solution will be replacement of the shale resins with synthetic plastics. (No references)

63-382 VIRUSES AND CANCER. (E.) Porter, G. F. (NCI, Bethesda, Md.). Arch. Intern. Me (Chicago) 111(5):572-591, 1963.

An historical survey of the known relationships between neoplasms and viruses and the major characteristics of the known oncogenic viruses have been presented. Possible mechanisms by which viruses produce cancer in animals are offered: viruses prevent the operation of normal growth controlling influences; viruses play primary or secondary roles in malignant transformations which require somatic mutations; viruses represent genic or potentially hereditary material (transduction or extrachromosomal mechanisms). The isolation of "infectious" DNA from polyoma virus-infected mouse cells has stimulated interest in transduction as a mode of carcinogenesis. Nucleic acid fractions, free of inhibiting DNA, might induce tumors. (242 references)

- 3-383 PIGMENTARY DISORDERS OF THE SKIN AND THEIR RELATION TO INTERNAL TUMORS. (E.) Curth, H. O. (Dept. Derm., Columbia U. Coll. Physicians Surg., New York). Ann. N. Y. Acad. Sci. 100(Pt. 1):76-91, 1963.

In a general review of the relationships between internal tumors and pigmentary dermatosis, the author classifies the pigmentation disorders into three types: those in which the dependence on the internal tumor has been established (Addison's disease, cachectic states, pseudo acanthosis nigricans), those in which dependence exists but does not explain the whole relationship between the 2 factors (malignant acanthosis nigricans), those in which neither component affects the other (Peutz-Jeghers syndrome), and those in which a regular association with internal tumors is suspected but not yet proved (unilateral verrucous nevi, vitiligo, urticaria pigmentosa). The genetic nature of both the monocutaneous melanosis and the g.i. polyposis in the Peutz-Jeghers syndrome is pointed out, and the variable sequence of development of the adenocarcinoma and malignant acanthosis nigricans is discussed. (37 references)

- 384 CARCINOMA OF THE SCROTUM: REVIEW OF LITERATURE AND PRESENTATION OF 2 CASES. (E.) Tucci, P. (Harlem Hosp., New York) and Haralambidis. J. Urol. 89(4):585-590, 1963.

Two cases of non-occupational carcinoma of the scrotum in Negroes are presented, believed to be the first ones reported in the USA. The etiology, incidence, pathology of scrotal carcinoma are discussed, as well as its clinical features. (10 references)

- 385 IMMUNITY AND HOST RESPONSE IN THE GROWTH OF TRANSPLANTED TUMORS. (E.) Jarck, J. V. Copenhagen, Munksgaard, 1962, 3 pp.

Experiments on the effect of irradiation on the growth rate of tumors obtained after implantation of primary or early-passage spontaneous mammary carcinomas, on the effect of cortisone treatment to C3H recipients of transplants of spontaneous mammary carcinomas, and on the transplantation of spontaneous C3H mammary carcinomas to homologous radiation-chimeras indicate that transplanted mouse carcinomas cannot be considered exclusively a phenomenon of proliferation of the implanted tumor cells. The formation of a transplanted tumor in the host is a reaction phenomenon since tumor growth depends also on host response, and tumor characteristics depend to an important degree on infiltrating elements of host tissue. Immunologic considerations lead to the concept that tumor formation is based on dynamic interaction between tumor graft and host response. If the tumor graft is antigenic to the host, the connective tissue response elicited is stimulated to develop a destructive phase. As new stromatization is interrupted, the tumor regresses. If the tumor graft does not exhibit antigenicity, but the tumor cells are so equipped as to evoke a host response, nonspecific connective tissue proliferation will occur. This results in a new stroma supply to the graft, which is then incorporated in the host and will grow progressively, provided it is continuously supported by a functioning host response to the unrejectable malignant element. The conclusion that nonspecific connective tissue reaction is a participating factor in the development of tumors may have broader implications especially in the field of chemical carcinogenesis. Cocarcinogens studied so far have one property in common, that of inducing hyperplasia and inflammation. (218 references)

- 63-386 CLINICAL OBSERVATIONS ON CANCEROUS CHANGE IN SKIN. (E.) Rank, B. K. (Royal Melbourne Hosp., Australia). Brit. J. Plast. Surg. 16(2):160-169, 1963.

In a general review and discussion, the author suggests that common skin cancers may be essentially the result of deficient reactivity of the dermal connective tissue, with consequent loss of the ability to contain and eventually eliminate epidermal invasion of the dermis (which is a normal component of the early stages of the healing process). This, combined with some surface breakdown, could create the conditions which may allow normal epithelial regeneration activity to go on to malignancy. He also suggests that keloid results from hyperreactivity of the connective tissue, and fibrosarcoma from extreme hyporeactivity. Details of some clinical cases are also presented to illustrate cancer in preexisting lesions, in radiation dermatitis and from junctional levi. (4 references)

See also abstract no.: 546

PHYSICAL CARCINOGENESIS

63-387 A POSSIBLE TWO-STAGE MECHANISM IN RHABDOMYOSARCOMA INDUCTION IN RATS.

(E.) Haran-Ghera, N. (Dept. Exp. Biol., Weizmann Inst. Sci., Rehovoth, Israel), N. Trainin, L. Fiore-Donati and I. Berenblum. Brit. J. Cancer 16(4):653-664, 1962.

Among 124 Wistar rats which received 700 or 1000 r over the liver area 7 days prior to three partial hepatectomies ten days apart, 31 tumors developed (20 sarcomas including 7 rhabdomyosarcomas). Among 126 rats irradiated following three partial hepatectomies, 12/21 tumors were sarcomas (including 1 rhabdomyosarcoma). X-ray treatment alone induced tumors in 3/116 (2 were sarcomas including 1 rhabdomyosarcoma). In 110 controls, 3 tumors were found, including 1 sarcoma. Fibrosarcomas and other malignancies were uniformly distributed, while the 9 rhabdomyosarcomas were all found in the abdominal scars (7 in rats treated with X-rays followed by hepatectomy). Mean latent periods were: 273 days for the rhabdomyosarcomas in group I, for fibrosarcomas in groups I and II, 600 and 536 days, resp. Incidence of metastasis among the induced malignant tumors was highest (7/9) for the rhabdomyosarcomas. The findings suggest a two-stage carcinogenic mechanism whereby radiation is the initiating factor and wound repair following repeated laparotomies acts as the promoting factor for rhabdomyosarcomas.

63-388 PROBABLE SARCOMA AND EPITHELIOMA ARISING ON A TUBERCULOUS LUPUS PREVIOUSLY SUBJECTED TO EXCESSIVE IRRADIATION. (Sp.) Vilanova, X. (Fac. Med., U. Barcelona, Spain) and A. Castell. Actas Dermosif. 53(6):325-340, 1962.

A 54-year-old man with a lesion of the cheek since age 19 treated intermittently with ointments then, at age 32, by intensive irradiation which caused edema and physical depression, presented with an ulcerated lesion of the same region. Histologically the tumor consisted of a well differentiated spinocellular epithelioma and a fusocellular sarcoma within a cicatrized lesion due to lupus vulgaris.

63-389 LEUKEMIA AFTER RADIOIODINE THERAPY FOR HYPERTHYROIDISM. (E.) McCormack, K. R. (Dept. Radiol., U. Calif. Sch. Med., San Francisco) and G. E. Sheline. Calif. Med. 98(4):207-209, 1963.

Between 1945 and 1960, among 650 pts. with hyperthyroidism treated with ^{131}I , 2 cases of leukemia occurred. In a 65-year-old woman chronic lymphatic leukemia was diagnosed 3 yr. after admin. of a total of 24.6 mC over a 4-month interval. A 48-year-old man developed acute or subacute myelomonocytic leukemia 14 yr. after treatment with 2.7 mC.

63-390 MALIGNANT HEMANGIOBLASTOMA INDUCED BY RADIATION. (Ger.) (Inst. Path., Essen Municipal Hosp., Germany). Legerlotz, C. Zbl. Allg. Path. 104(1/2):58-66, 1962.

Case report of a 52-year-old woman who was admitted with a 2 yr. history of hemangioblastoma on the lower abdomen, approx. 12 yr. after a radical hysterectomy for squamous-cell carcinoma of the cervix. The operation was preceded by radium therapy and over a period of 1-8½ mo. after the operation she received X-ray therapy (2400 r to 2 abdominal and 2 gluteal regions, 660 r to a vulval region and 2200 r to a sacral region). Approx. 3-5 weeks later, swelling of the inguinal lymph nodes appeared, and the lesions were excised. Detailed macroscopic and microscopic examination revealed no recurrence of carcinoma, but a typical malignant hemangioblastoma with metastasis to the lymph nodes. The site of the lesions, the latent period before their development and the X-ray dosage admin. confirm the supposition that this malignancy was induced by radiation.

63-391 STUDIES OF THE LATE EFFECTS OF INTERNAL IRRADIATION BY RADIOACTIVE STRONTIUM IN THE RAT. (E.) Kahn, D. S. (Dept. Exp. Surg., McGill U., Montreal, Canada), J. S. Makhani and S. C. Skoryna. Laval Med. 34(1):169-183, 1963.

In rachitic animals with experimental fractures of the femur, uptake of Sr^{89} at the fracture site remained high during the stage of active healing; by the time complete healing occurred, no significant radioactivity remained. However, when healing or remodeling failed to occur normally, a failure of the reversal of retention of the isotope was also observed, and some tumors developed at the fracture site after a latent period of 260 days. Included is a general review (41 references) of radioactive strontium which includes general considerations, effects on bone tissue, uptake and turn-over, effects of low calcium intake as well as hormonal effects. The authors also noted that from previous experiments in rats given single inj. of Sr^{89} (0.001-1.0 $\mu\text{C/g}$ body wt. i.p.), no tumors or radiation osteitis occurred during the 24 mo. observation period. After admin. of 2 $\mu\text{C/g}$ or higher doses, malignant bone tumors were found in some rats which survived for 1 yr. or more; mortality was high. Intermittent doses of Sr^{89} (0.1 $\mu\text{C/g}$ x 2/week to a total of 20 i.p. inj.), produced no tumors; 36 inj. proved toxic and survivors showed only micro tumors. After 40 inj., mortality was high but tumors were frequent in survivors; of the animals that survived 50-53 inj., tumors developed consistently in the metaphyseal region beginning 260 days after the initial admin. These results indicated that the neoplastic response is a function of both the conc. and time of exposure to radioactive strontium.

3-392 EFFECTS OF CHRONIC MICROWAVE IRRADIATION ON MICE. (E.) Prausnitz, S. Electronics Res. Lab., U. Cal., Berkeley) and Süsskind. IRE Trans. Biomed. Electronics BME (2):104-108, 1962.

Exposure of male Swiss albino mice to chronic 2.2-cm microwave irradiation (0.100 w/cm² for 5 min. a day, 5 days/week) for 59 weeks raised the body temperature by an av. of 3.3°C but had no significant effect on survival time, body wt., response of body temperature to heating, or blood picture. Autopsy studies on mice which died spontaneously or were sacrificed at 19 mo. (but not those sacrificed at 7 or 16 mo.) revealed testicular degeneration, with atrophy of the tubules and decreased spermatogenesis in a high proportion (38-40% of irradiated mice and 5-8% of controls). The mice which died spontaneously and those sacrificed at 16 mo. also showed a high incidence of leukosis, manifesting as either monocytic or lymphatic leukosis or lymphatic or myeloid leukemia (30-35% of irradiated and 10% of control mice). Exposure to LD₅₀ doses (9 g. daily at the same intensity) increased the body temperature by an av. of 6.7°C but did not impair the fertility of the survivors.

3-393 THE EFFECT OF RADIATION DOSAGE ON THE INCIDENCE OF HEMATOPOIETIC NEOPLASMS IN MICE. (Rus.) Aleksandrov, S. N. (Cent. Radiol. Inst. Min. Health USSR, Leningrad) and K. F. Galkovskaia. Vop. Onkol. 9(3):40-44, 1963.

The effect of radioactive Co, 3.7 milliroentgen (mr)/minute, 87 mr/minute, and 23 r/minute, upon the development of thymus lymphosarcoma (LS), and leukemias (L; myeloid and lymphoid), was studied in random-bred mice. The optimum dose for LS was 87 mr/minute; increasing or decreasing the dose resulted in a decreased incidence of LS. The incidence of L increased with the dose, but on reaching the maximum at 87 mr/minute, it remained unaltered, although doses other than 87 mr/minute primarily induced the myeloid forms. The latent period for LS and L (lymphoid) was the same at both 23 r/minute and 87 mr/minute, but the latent periods of L was somewhat longer than for LS; a decrease was noted with 3.7 mr/minute. The latent period for L (myeloid) was not dose-dependent.

3-394 THE INCIDENCE OF LYMPHOSARCOMA IN MICE SUBJECTED TO SINGLE OR FRACTIONATED DOSES OF RADIATION. (Rus.) Aleksandrov, S. N.

(Cent. Radiol. Inst., Leningrad) and K. F. Galkovskaia. Dokl. Akad. Nauk SSSR 146(5): 1189-1192, 1962.

When mice weighing 18-20 g were subjected to whole-body γ -irradiation at a total dose of 800 r and a rate of 23 r/minute (in a single dose), lymphosarcomas appeared in 6/103 males and 3/135 females surviving at least the minimal latent period (205 and 162 days, resp.). After 4 doses of 200 r at 7-day intervals, lymphosarcoma appeared in 12/370 males and 28/318 females which survived the minimal latent period (205 and 162 days, resp.). Incidence after 4 x 200 r at 30-day intervals was 8/92 females which survived at least 128 days; no tumors appeared in controls or in irradiated males. The coefficient of carcinogenic effectiveness (representing the number of tumors x the av. latent period divided by the number of mice surviving the minimal latent period x the av. life span following the minimal latent period) and the av. latent period in days, were, for those given a single dose, 0.100 and 269 (males) and 0.029 and 215 (females); for those given 4 doses, 0.043 and 224 (males) and 0.085 and 223 (females); for females irradiated at 30-day intervals, 0.122 and 183. In all cases but 1 (having lymphosarcoma of the mesenteric lymph nodes), the tumors were localized in the thymus. The sex difference is explained by the oncogenic effect of estrogens and onco-static effect of androgens, the gonads being destroyed most effectively by a single large dose of irradiation. (See preceding abstract.)

63-395 ACUTE LEUKEMIA FOLLOWING RADIOTHERAPY FOR MALIGNANT TUMORS. (REPORT OF TWO CASES.) (Fr.) Michon, P., A. Larcen, F. Streiff, A. Peters and P. Canton. Ann. Med. Nancy 2:136-142, 1963.

Following a review of the literature on the appearance of leukemia as a result of irradiation, the authors report 2 cases which were rapidly fatal. In both cases, the original tumors were apparently cured and did not recur, the pts. dying of a particularly virulent leukemia marked by severe anemia and thrombocytopenia. In the first case, a 56-year-old woman developed acute lymphoblastic leukemia (WBC = 160,000) 17 mo. after mastectomy and 40 X-ray treatments to axillary, thoracic and cervical fields. In the 2nd case, a 49-year-old man developed acute myeloblastic aleukemic leukemia approximately 3 yr. after castration (for seminoma) and 150 X-ray treatments.

See also abstract nos.: 366,385,386

CHEMICAL CARCINOGENESIS

63-396 SPECIES DIFFERENCES IN PENETRATION AND ABSORPTION OF CHEMICAL CARCINOGENS.

(E.) Bock, F. G. (Roswell Park Mem. Inst., Springville, N. Y.). Nat. Cancer Inst. Monogr. (10):361-375, 1963.

High degrees of penetration of 1% solutions (in benzene) of 9,10-dimethyl-1,2-benzanthracene, 3,4-benzpyrene (BP) and 20-methylcholanthrene were observed into the clipped skin of mice, hamsters and rabbits, with much lower degrees in guinea pigs, rats and man; these differences correspond with the reported sensitivities of these species to topically applied carcinogens. In mice, hair growth pattern seemed to have little effect on the penetration of BP. The concentration of BP in the skins of DBA/1 or F mice was 3 times that in A or ICR Swiss; this may indicate genetic control over the skin structure, since BP penetrated as well into dead mouse skin as into live skin. In most strains, penetration was the same in males and females, but 4 strains showed higher rates in male skin. In structure-activity studies, the rate of penetration was favored by small molecular size and high solubility in nonpolar solvents, as well as by the presence of a volatile solvent. These data on penetration of hydrocarbons, as well as data on the relative thickness of the skin in different species and at different sites, indicate that differences in susceptibility to carcinogenesis may be due to physical differences in the pathway by which the carcinogen reaches the target cells.

63-397 INEFFECTIVENESS OF AUTOTRANSPLANTATION ON GROWTH OF THE METHYLCHOLANTHRENE SARCOMA IN RATS AND MICE. (E.) Matsuyama, M. (Dept. Path., Nagoya City U. Sch. Med., Japan), A. Maekawa, H. Horikawa, K. Suzumori, K. Soqa and K. Iwai. Nature 197:805, 1963.

20-Methylcholanthrene (3 mg in rats and 1 mg in mice, s.c.) led to the development of fibrosarcomas in 100-130 and 70-100 days, resp. In some animals, when the tumors had reached a diameter of 20-25 mm (rats) or 12-15 mm (mice), 2/3 of the tumor was excised and slices of each animal's own tumor were reimplanted (s.c. in rats; i.p. in mice). Neither type of autotransplantation had any significant effect on the growth of the remaining tumor or on the average survival-time of the hosts (47-50 days in rats and 36-39 days in mice).

63-398 EXPERIMENTAL LUNG CARCINOMA IN ANIMALS PRODUCED BY BENZPYRENE. (Ser.) Milicevic, D. (Oncol. Inst., Fac. Med., Belgrade). Srpski Arh. Celok. Lek. 90(10):917-922, 1962.

One group of 15 rats was thoracotomized, after which benzpyrene (BP; 5 mg) was introduced into the parenchyma of the lung through the visceral

pleura. A second group of 15 rats got only the carcinogen, introduced into one of the bronchi via an orotracheal filliform bougie. In the 2 groups, there were 8 operative deaths. Nine mo. after BP admin., a planocellular carcinoma had developed in the lung of a surviving rat in the first group. Tumors showing precancerous changes were found in 1 rat dying at 5 mo. (group 1) and in another pulmonectomized at 7 mo. (group 2). Expectoration of the carcinogenic material is regarded as the reason for the arrest of the neoplastic process in the precancerous stage in the majority of the animals.

63-399 DIFFERENTIAL RESPONSES OF PARAMECIUM AURELIA TO CIGARETTE COMPONENTS. (E.) Wang, H. (Stritch Sch. Med., Loyola U., Chicago). Nature (London) 197:946-948, 1963.

Exposure of a kappa-less strain of P. aurelia to either the tobacco, mainstream smoke, whole ash or paper ash from 7 brands of nonfilter cigarettes resulted in decreased survival time in all cases. The tobacco itself was consistently the most toxic, followed by mainstream smoke, whole ash and paper ash, with insignificant differences between brands; toxicity was higher at 31°C than at 23°C. With tobacco or smoke, all the paramecia died, while with ash (whole or paper), 10-20% survived; these differences may be due either to somatic superiority or genetic characteristics. Both tobacco and mainstream smoke had a powerful tranquilizing effect; tobacco, however, produced slight shrinkage and an ectoblastic blister at one pole of the animal, while smoke produced swelling and endoplasmic clumping. Both types of ash had a stimulatory effect, producing abnormal motility patterns; both produced many intracellular pathological changes. The greater toxicity of the paper ash may be related to the use of higher combustion temperatures than would occur in normal smoking. The possible similarities between paramecia and ciliated respiratory epithelium are pointed out.

63-400 BRONCHIAL ADENOMATOSIS INDUCED IN RABBITS BY I.V. INJECTION OF CARBON TETRACHLORIDE. (Rum.) Ghera, G., L. Gavrilita and I. Pojoga. Stud. Cercet. Stiint. (Med.) 13(1):123-129, 1962.

After a single dose of CCl₄ (0.03 or 0.05 ml/kg i.v.), rabbits were observed for a maximum of 20 days. Macroscopic inspection of lungs from rabbits surviving less than 5 days showed increased volume, rounding of the margins, cherry-colored parenchymal consolidations, and generalized congestion. In rabbits surviving for a longer period, there was less congestion. Microscopically, the lungs showed various types of lesions, depending on the time of death after CCl₄ treatment. Rabbits surviving less than 5 days showed edematous and hemorrhagic alveolitis; those

dyling after 8-10 days showed less intensive alveolitis, incipient resorption of hemorrhagic foci and their replacement by newly-formed connective tissue. Later, two kinds of histopathologic change were consistently observed: (1) inflammatory lesions with zones of consecutive necrosis, and (2) proliferative lesions of the bronchial epithelium. There was a strict correlation between pulmonary parenchymal necrosis and bronchopulmonary adenomatosis; the latter never appeared in the absence of the former. The similarity of the histologic picture of CCl₄-induced bronchial adenomatosis to that of experimental adenomatosis, spontaneous or induced by other agents and to that of human pulmonary adenomatosis was striking.

3-401 CIGARETTE PAPER, SMOKER'S COUGH, AND LUNG-CANCER RISK. (E.) Loxton, G. E. (Brook Hosp., London). *Lancet* 1:834-835, 1963.

In a letter to the editor, the author reports on 25 pts. (34 with lung cancer): 124/225 had coughs; the coughers included 7/25 who did not smoke, 63/101 who smoked machine-rolled (packet) cigarettes, and 54/99 who smoked hand-rolled cigarettes. The 3 brands of cigarette papers used differed in wt., ultra-violet fluorescence, and ash content (17%, 9.2%, and 8.6%, resp.). It appears that the incidence of smokers' cough, and lung cancer risk, rise with the inorganic content (ash) of the cigarette paper; of the 34 lung cancer cases, only one used the low ash content cigarette paper.

-402 URETHAN (ETHYL CARBAMATE) AS A MULTIPOTENTIAL CARCINOGEN IN BALB/c, AND Db FEMALE MICE. (E.) Ida, N. (Dept. Mediat., Okayama U. Med. Sch., Japan), N. Oda, Yoda and T. Kiyama. *Acta Med. Okayama* (4):253-264, 1962.

Female mice, Balb/c, Zb, or Db were divided into groups as follows: a) controls, b) urethan (U; 500 mg/g i.p. every 4 days x 11, starting at 5 weeks), c) U + mammary tumor extract (MTE; 0.5 i.p. at 8-9 weeks, cell free extract consisting of mixed spontaneous C3H, Db, Stoll, C58, and F₁ hybrid tumors, and of Fn-methylcholanthrene-induced tumors in the NH and Db strains), and d) MTE alone. In the Balb/c strain spontaneous lung tumors developed in 5% of 62 animals at a mean age of 670 days. Treatment with U increased the incidence to 100% (29/29), and accelerated the time of tumor appearance to a mean age of 469 days; MTE induced lung tumors in 7/27 (26%), appearing on the av. at 533 days. When the animals were treated with U + MTE, lung tumors were induced in 26/32 (81%), but there were also ovarian cysts, 2 leukemias (including 1 mediastinal lymphoma), 1 mammary cancer and 1 hepatoma, as well as hemorrhagic lesions of various organs. Zb strain controls had a spontaneous tumor incidence of 2% lung, 5% leukemia, 2% mammary cancer and no hepatomas,

developing at a mean age of 442 days. Treatment with U increased the tumor incidence to 71% lung, 21% leukemia (all with mediastinal lymphoma), 4% mammary tumors and 18% hepatoma, while MTE caused only leukemias 2/27 mice (1 with mediastinal lymphoma). Animals treated with U + MTE had the same tumor distribution as those treated with U alone, except for a higher (32%) incidence of hepatomas. In all 3 treated groups there was a high incidence of hemorrhagic lesions. The Db strain showed a low rate of spontaneous tumors: 1% lung, 12% leukemia, 7% mammary cancers and no hepatomas, developing at an av. age of 564 days. U treatment increased the lung cancer incidence to 44% (11/29), leukemia to 28% (7/29), and of hepatoma to 20% without affecting the mammary tumor frequency. MTE increased mammary tumor frequency, to 31% (1 (4%) showed a mediastinal lymphoma). However, animals receiving U + MTE extract had a variety of tumors including lung (32%), leukemia (38%, including 32% lymphomas), mammary cancer 26% and hepatoma (6%). The first and third group also showed a high incidence of hemorrhagic lesions. Results suggest that U is a multipotential carcinogen in the induction of various tumors in the 3 mouse strains.

63-403 ON THE VALUE OF A FLUORESCENCE INDEX IN STUDIES OF AIR POLLUTION. (Fr.) Rondia, D. (Toxicol. Lab., U. Liege, Belgium). *Arch. Belg. Med. Soc.* 20(9-10):567-578, 1962.

Filter papers exposed to air in 6 areas for 6 mo. were extracted in a Soxhlet, concentrated and examined in a fluorimeter at 480 mμ. Aliquots of the same soln. were separated on an aluminum oxide column and the various polycyclic hydrocarbons determined quantitatively against known standards. Detailed statistical analysis showed some lack of homogeneity in samples obtained from different locations, with 1 of 6 samples showing considerably lower correlation to analytical results than the remaining samples. There was also a definite seasonal variation in the correlation between analytical and fluorescence studies, probably due to variations in the respective contribution of fumes from domestic heating plants and from automobiles.

63-404 EPITHELIOMAS OF ARSENICAL ORIGIN. (Fr.) Tello, E. E. (Fac. Med., Cordoba Natl. U., Argentina). *Rev. Fac. Cienc. Med. Cordoba* 20(3):197-206, 1963.

While there is little danger of occupational arsenic toxicity, chronic environmental arsenic poisoning still occurs in the province of Cordoba, Argentina due to the drinking of artesian well water with a high arsenic content. The syndrome "endemic regional chronic hydro-arsenicalism" develops after puberty in predisposed individuals, in the form of a dermatosis showing consistent transformation into epitheliomas. The initial lesions can only be identified by histologic study; later, 2 characteristic types of pre-

epitheliomatous lesion are seen: melanodermas and keratodermas. The multiple epitheliomas develop at the affected sites, as a result of spontaneous evolution of the keratotic lesion, or due to the direct carcinogenic effect of the arsenic, or because of chronic irritation by arsenic deposits in the upper layer of the dermis. Of 175 pts. examined since 1942, 40 had Bowen's disease (including 8 with Bowen's cancer). In the author's opinion, Bowen's disease (for which an arsenical origin has also been postulated) and multiple superficial epitheliomas rarely develop in the absence of chronic arsenical dermatitis.

- 63-405 FILTRABLE VIRUS-LIKE AGENT ISOLATED FROM TUMOURS INDUCED BY CARCINOGENIC SUBSTANCES. (E.) Ageenko, A. I. (Hertzen State Oncol. Inst., Moscow). *Folia Biol. (Praha)* 8(1):7-11, 1962.

Cell-free extracts of 20-methylcholanthrene or 9,10-dimethyl-1,2-benzanthracene (DMBA)-induced tumors in C57Bl mice, when admin. i.p. to 581 mice 1-6 days old, induced tumors in 45 (15.7%) of the 285 surviving mice, with an av. latency of 8.6 mo. These extracts were effective only when prepared from tissues taken less than 30 days after the primary tumor became palpable. Repeated i.p. and intracerebral passages enhanced the pathogenic properties of the agents. Also, chemical carcinogenesis (by DMBA) was enhanced and hastened by the cell-free extract (0.5 ml/week x 2) from DMBA-induced tumor tissue. Tumors were larger than in the controls, and became palpable sooner. This substance had many characters of a virus. It could be maintained at -14 C for 2 weeks, in 50% neutral glycerine for 2.5 mo., but was inactivated by heating to 80 C for 30 min.

- 63-406 THE EFFECTS OF DIETARY DEFICIENCIES ON THE PENETRANCE OF MELANOTIC TUMOURS IN *DROSOPHILA MELANOGASTER*. (E.) Sang, J. H. (A.R.C. Poultry Res. Ctr., Edinburgh, Scotland) and B. Burnet. *Experientia* 18(Pt. 1):127-128, 1963.

In *Drosophila*, under axenic conditions, reduction of dietary RNA, cholesterol or biotin between 45 and 50 hr. after hatching increases the penetrance of the *tu* gene for melanotic tumor formation. The RNA effect is due to a shortage of adenylic acid, and is dependent on the dietary adenylic/cytidylic balance. At threshold amounts of RNA, suboptimal supplies of thiamine, pyridoxine, and folic acid, all increase tumor penetrance by interfering with *de novo* synthesis of adenylic acid. High tumor penetrance from cholesterol or biotin deficiency is not reduced significantly by increasing the RNA supply, suggesting that the 3 effective treatments operate through different metabolic routes to produce the same phenotype.

- 63-407 A STRAIN COMPARISON OF TUMORIGENIC RESPONSES IN *DROSOPHILA MELANOGASTER*. (E., Abstract) Burnet, B. (A.R.C. Poultry Res. Ctr., Edinburgh, Scotland) and J. H. Sang. *Experientia* 18(Pt. 1):128, 1963.

Both *tu k* and *tu bw;st Su-tu* strains of *Drosophila melanogaster* showed low penetrance to melanotic tumor formation. Both strains produced tumors when fed excess tryptophan, but only the latter responded to x-irradiation of the egg. Crosses between the strains behaved differently according to treatment. Chromosome analysis showed that, although both strains carry *tu* genes in chromosome 11, other modifying genes (including suppressors) affect penetrance and phenotypic expression. (See also preceding abstract.)

- 63-408 FREE PHENOLIC ACIDS IN CIGARETTE SMOKE AND TOBACCO. PAPER CHROMATOGRAPHY: SEPARATION AND IDENTIFICATION. (E.) Yang, C.-H. (Chem. Dept., U. Oklahoma, Norman) and S. H. Wender. *J. Chromatogr.* 8(1):82-89, 1962.

The smoke of regular market cigarettes and of cigarettes prepared without the usual flavorings or other additives contained the following free phenolic acids: m-hydroxybenzoic, p-hydroxybenzoic, protocatechuic, vanillic, syringic, p-hydroxyphenyl-acetic, m-hydroxyphenyl-acetic, o-hydroxyphenyl-acetic, p-coumaric, ferulic, m-hydroxyphenyl-propionic, and p-hydroxyphenyl-propionic. The ether and ethyl acetate extracts of tobacco from both types of cigarettes contained the same acids. Paper chromatography separation and identification procedures are described.

- 63-409 PRECURSORS OF CARCINOGENIC HYDROCARBONS IN TOBACCO SMOKE. (E.) Gil-av, E. (Weizmann Inst. Sci., Rehovoth, Israel) and J. Shabtai. *Nature (London)* 197:1065-1066, 1963.

Analysis of the products of isoprene pyrolyzation at 600°C (3-second contact time) and at 610°C (4-second contact time) revealed 3,4-benzpyrene in 0.1% and 0.15% of the tar, resp. These and other results obtained from the literature have led the authors to propose the following pathway for the formation of polycyclic aromatics in burning tobacco: solanesol and other isoprene formers → isoprene → dipentene and isomers, which may be split or dehydrogenated to yield C6-C10 alkylbenzenes, or condensed to give polycyclics, including 3,4-benzpyrene. The alkylbenzenes may also condense to yield polycyclic compounds.

- 63-410 SOME DIETARY FACTORS IN EXPERIMENTAL LIVER CANCER. (E.) Eversole, W. J. (Div. Sci., Indiana State Coll., Terre Haute) and C. Bianciflori. *Lavori Inst. Anat. U. Perugia* 22(3):197-202, 1962.

Mature Wistar rats fed a complete stock diet

cluding riboflavin for about 4 mo. failed to develop liver tumors. After addition of 3'-methyl-4-dimethylaminoazobenzene (3'-Me-DAB; 0.06%), 5/5 males and 4/6 females developed liver lesions; 4 of the males, but no females developed liver carcinomas. Further addition of a riboflavin antagonist, 6,7-dimethyl-9-(2'-acetoxyethyl)-xanthoxazine (U 2112; 20 mg/kg of diet x 3 weeks, then 1 g/kg x 5 weeks) appeared to inhibit the development of liver lesions and carcinoma; the only lesions seen were whitish, blotchy ones in 5 males.

-411 ALVEOLAR HYPERPLASTIC NODULES AND MAMMARY TUMORS IN LOBECTOMIZED VIRGIN MALE MICE (BALB/cf/Cb/Se SUBSTRAIN). (It.) Schera, F. (Inst. Anat. Pathol. Hist., U. Perugia, Italy). Lavori Inst. Anat. Univ. Perugia 22(3):189-195, 1962.

ginal smears and histological studies of the mammary glands, ovaries and uteri of 31 virgin male mice of the BALB/cf/Cb/Se substrain, either allowed to live to a normal lifespan or killed after the appearance of mammary tumors. Irregularities in the estrus cycle, showed at extirpation of the olfactory lobe at the age of 2 mo. completely prevented the appearance of pseudopregnancy. Nevertheless, alveolar hyperplastic nodules were found in the breasts of 4 mice (including 1 without a tumor), and mammary adenocarcinoma was detected in 8/24 mice allowed to live more than 6 mo. The first tumor appeared at 9 mo. of age, and 5 of the 8 appeared between the 13th and 15th mo. It thus seems that a high percentage of mammary tumors arise from preformed alveolar hyperplastic nodules, even in the absence of pseudopregnancy.

-412 CARCINOGENIC SUBSTANCES IN WATER AND SOIL. XII. POLYCYCLIC AROMATIC HYDROCARBONS IN SURFACE WATERS. (Ger.) Neff, J. (Inst. Hyg., Johannes Gutenberg-U., Mainz, Germany) and R. Fischer. Arch. Hyg. Bakt. (8):572-585, 1963.

omatographic studies (alumina columns and paper chromatography using mixtures of benzene and cyclohexane) on benzene extracts of the centrifuged sediment from Rhine river water and filter sludge from rapid filtration units on Lake Constance revealed 19-25 fluorescent substances; the total content of polycyclic aromatic hydrocarbons was 8-10 mg/kg dry matter, 62 g of sediment being obtained from 2.7 cubic meters (m³) of Rhine water. The carcinogens 1-benzopyrene, 3,4-benzofluoranthene, 10,11-benzofluoranthene, 1,2-benzanthracene, chrysene, indeno(1,2,3,cd)pyrene, and the non-carcinogenic hydrocarbons fluoranthene, pyrene, 11,12-benzofluoranthene and 1,12-benzperylene were positively identified. Among the other 15 compounds, many of which were present in very small amounts, 2 were probably dibenzanthracene and dibenzpyrene. Calculations showed that the

concentration of carcinogenic hydrocarbons in mg/m³ of untreated water amounts to 0.075 for Rhine river water and 0.0003-0.0004 for water from Lake Constance. This indicates that drinking water, especially if not treated with activated charcoal, should not be neglected as a source of contamination with carcinogens.

63-413 LUNG CARCINOGENESIS BY URETHANE IN NEWBORN, SUCKLING AND ADULT SWISS MICE. (E.) De Benedictis, G. (U. Bari, Italy), G. Maiorano, L. Chieco-Bianchi and L. Fiore-Donati. Brit. J. Cancer 16(4):686-689, 1962.

Of 80 newborn Swiss mice, injected once with urethan (U; 2 mg, s.c.) and killed at 20, 45, 90, and 210 days of age, lung tumors were found in 4/20, 5/20, 15/15, and 25/25, resp.; mean nodule counts were 1, 2, 5, and 17, resp. Of 83 adult mice similarly treated at age 45 days, lung tumors developed in 0/31, 4/16, 12/15, and 19/21 at 20, 45, 90, and 210 days, with mean nodule counts of 0, 1, 3.5, and 4, resp. Another group of 91 mice, themselves not treated but nursed by mothers which received 3 mg of U by stomach tube in 0.25 ml of water 1, 3, and 5 days after parturition, developed tumors as follows: 0/18 at 20 days, 2/20 at 45, 11/21 at 90, and 25/32 at 210 days, with mean nodule counts of 0, 1, 2, and 2, resp. When a similar group of 66 young were caged with their U-treated male parents, only 3/26 developed tumors at 210 days, with a mean nodule count of 1. A group of 174 untreated controls developed spontaneous tumors in 5/74 but only at age 210 days, with a mean nodule count of 1. Thus, U admin. to lactating mothers induced lung tumors in many of their offspring, not through environmental contamination but by U excretion in maternal milk.

63-414 A SHORT TERM TEST FOR CARCINOGENICITY. THE EFFECTS OF CERTAIN CLOSELY-RELATED POLYCYCLIC AROMATIC HYDROCARBONS ON EMBRYO TISSUE HOMOGRAFTS IN BALB/c STRAIN MICE. (E.) Peacock, P. M. (Roy. Beatson Mem. Hosp., Glasgow, Scotland) Brit. J. Cancer 16(4):701-706, 1962.

A new simple method is reported for testing the carcinogenicity of a small amount of any substance (less than 150 µg) in a short time (16 weeks). BALB/c mouse embryonic stomach, lung, skin or bladder were implanted in the thigh muscle of adults of the same strain where they survived and differentiated normally. Since inclusion of small quantities of carcinogenic hydrocarbons in close apposition to separate embryo grafts can induce malignant tumors in the implants, 13 hydrocarbons (8 pyrenes and 5 anthracenes), were tested by this method. Of 9 previously reported to be carcinogenic, 7 induced tumors in embryo implants: 3,4-benzopyrene, 1,2,3,4-, 1,2,4,5-, 3,4,8,9-, and 3,4,9,10-dibenzopyrene, 1,2,5,6-dibenzanthracene and 1,2,7,8-dibenzanthracene. The 2 previously reported carcinogens which were negative were anthracene and 1,2-benzanthracene. Pyrene and

1,2-benzpyrene, previously reported as non-carcinogenic, and 1 untested compound, 1,2,6,7-dibenzpyrene, induced no tumors. The tumors were usually squamous carcinomas, but sarcomas were also observed.

- 63-415 STUDIES ON TRICYCLOQUINAZOLINE CARCINOGENESIS: INTERACTION OF CARCINOGEN WITH SKIN COMPONENTS. (E.) Baldwin, R. W. (Cancer Res. Lab., U. Nottingham, England), H. C. Palmer and M. W. Partridge. *Brit. J. Cancer* 16(4):740-748, 1962.

Tricycloquinazoline (TCQ) painted on mouse skin did not appear to bind firmly with skin components. Examination of whole skin samples and of their fractions during various stages of carcinogenesis also demonstrated a lack of firm binding to nucleic acid or protein fractions. TCQ also failed to interact with phospholipid and, although the neutral fat fraction contained TCQ, the carcinogen was shown not to be associated with any particular lipid fraction. The present results together with evidence on the variation of TCQ carcinogenicity following structural changes (primarily at position 2) suggest that the primary interaction of carcinogen and tissue involves multiple low energy bonding with a highly specific tissue receptor site.

- 63-416 PROTEIN-BOUND DYES IN THE SERUM AND LIVER OF RATS FED AMINOAZO DYES. (E.) Dijkstra, J. (S. African Council Sci. Indust. Res., Pretoria) and T. B. Louw. *Brit. J. Cancer* 16(4):757-762, 1962.

The extent of binding of dye to proteins was determined in the liver and serum of rats after intragastric admin. of a single dose of 50 mg of various aminoazo dyes to male albino Wistar rats. The free, alcohol extractable dye levels of 3'-methyl-4-dimethylaminoazobenzene (3'-MeDAB) and 2-methyl-4-dimethylaminoazobenzene (2-MeDAB) in both serum and liver were low during the first 10 hr., rose to a maximum after 20-40 hr. and then declined. The appearance of the bound dye in the liver and in the serum followed parallel courses. The extent of binding of the various dyes to proteins in the liver paralleled their carcinogenicity, except in the case of 2-MeDAB, which is a weak carcinogen but was strongly bound. For 3'-MeDAB, 4-dimethylaminoazobenzene, 2'-methyl-4-dimethylaminoazobenzene, 4-diethylaminoazobenzene, and 4-aminoazobenzene the ratio of bound dye (in optical density units) per unit weight of protein in the serum to that of the liver averaged 0.5, whereas with 2-MeDAB it was only 0.19. The binding of 2-MeDAB to serum proteins is therefore more in line with its low carcinogenicity than its binding to liver proteins.

- 63-417 INDUCTION OF MALIGNANT TUMORS IN THE GUINEA PIG BY ORAL ADMINISTRATION OF DIETHYLNITROSAMINE. (E.) Argus, M. F. (Dept.

Med., Tulane U. Med. Sch., New Orleans, La.) and C. Hoch-Ligeti. *J. Nat. Cancer Inst.* 30(3):533-551, 1963.

Diethylnitrosamine (DEN) given in the drinking water, induced from the 16th week onward hepatic carcinomas in 14/15 hybrid guinea pigs. Drug dosage (varied to adjust to water intake), av. 1-2 mg/day during the major portion of 2 experiments lasting 40 and 34 weeks (360 mg - 290 mg total, resp.). The majority of tumors were of trabecular carcinomatous or adenocarcinomatous pattern, or both; 1 sarcomatous and several anaplastic tumors were seen. The tumors invaded the lymphatic and blood vessels and metastasized to the lymph nodes, omentum, lung, kidney and adrenal. Hyperplasia of the mucosa and 1 adenocarcinoma of the gallbladder occurred. In the large bronchi, squamous metaplasia and 2 squamous papillomas were observed. Multiple nodules of peripheral bronchiolar tumor were present in 7 animals.

- 63-418 INDUCTION OF BACTERIOPHAGE FORMATION IN LYSOGENIC BACTERIA BY A POTENT CARCINOGEN, 4-NITROQUINOLINE 1-OXIDE, AND ITS DERIVATIVES. (E.) Endo, H. (Cancer Res. Inst., Kyushu U., Fukuoka, Japan), M. Ishizawa and T. Kamiya. *Nature (London)* 198:195-196, 1963.

4-Nitroquinoline 1-oxide, 6-chlor, 4-nitroquinolin 1-oxide, 4-hydroxylaminoquinoline 1-oxide, and 4-nitroquinaldine 1-oxide, all known carcinogens, had inducing activity in *Escherichia coli* K12 (λ) exposed for 10 minutes to 1×10^{-4} - 2.5×10^{-5} M. At the same concentrations the following non-carcinogenic compounds failed to induce bacteriophage formation: 4-nitroquinoline, 4-nitropyridine 1-oxide, quinoline 1-oxide, 4,6,8-trinitroquinoline 1-oxide, 4-(S-cysteinyl)quinoline 1-oxide and 4-aminoquinoline 1-oxide. Thus, in this series there was complete coincidence between carcinogenicity and ability to induce *E. coli* K12 (λ). But from earlier negative data on di-methylnitrosamine it seems difficult to say that inducing action is a character common to all water-soluble carcinogens.

- 63-419 STATISTICAL CONCLUSIONS ON SOME NEOPLASMS OF THE LARYNX. (Sp.) Farjat, F. P. (Inst. Oto-Rhino-Laryngol. Service, San Martin Polyclin., Argentina), C. A. Salvatore and A. P. Greco. *Prensa Med. Argent.* 49(33):1739-1741, 1962.

Of 100 white pts. with cancers of the larynx seen at the San Martin Polyclinic in Argentina, 92/98 males were smokers, mostly of black cigarillos (83% of smokers, average 31/day); both females were smokers. Family history of cancer was positive for cancer of the larynx in 5, for cancer of other organs in 4, and doubtful in 3. Age distribution for 78 pts. was: below 34, 2.5%; 35-44, 3.6%; 45-54, 25%; 55-64, 42%; 65-74, 24%; and 75-or over, 1%.

420 DISCREET SEPARATION OF POLYCYCLIC HYDROCARBONS IN AIR BORNE PARTICULATES USING VERY LONG ALUMINA COLUMNS. (E.) Cleary, J. (Sch. Chem. Technol., U. New South Wales, Sydney). *J. Chromatogr.* 9(2):204-215, 1962.

A method is described for the distinct separation and identification of polycyclic hydrocarbons, using long alumina columns (26.5 x 0.5 in.), then, assay. As a typical example of its value in air pollution assays, chromatograms are given for compounds identified by this method in an air sample collected on a roof in Sydney, Australia. From a solid deposit of 2.011 g (from 422,500 cubic ft. of air passing at 50 cubic ft./minute), fractions were obtained after extraction and column chromatography. Polycyclic hydrocarbon concentrations in the solid (p.p.m.) were: naphthalene 3.9; anthracene 2.8; pyrene 15.2; fluoranthene 17.9; 9:10-benzophenanthrene 14.2; 1:2-benzanthracene 3.5; chrysene 20.1; 1:2-benzpyrene 18.8; 3:4-benzpyrene 20.7; 2:3-benzofluoranthene 3.0; 1:12-benzoperylene 21.8; phenanthrene 8.0; and coronene 15.9.

421 EXCITATION TRANSFER AND CARCINOGENESIS. (E.) Pullman, A. (Inst. Biol. Phys.-Chem., Paris) and H. Berthod. *Biochim. Biophys. Acta* 66(2):277-279, 1963.

It had been suggested by others that cancer induction by conjugated hydrocarbons might be the result of a transfer of excitation energy by resonance from tryptophan to the carcinogen, after formation of a protein-carcinogen complex; an equation (J₁) for the probability of such dipole-dipole energy transfer being proportional to the overlap integral had been formulated. To check on the validity of this energy transfer hypothesis, the J₁ values were calculated for 21 hydrocarbons (plus a new evaluation of 1,2-benzanthracene) in addition to 5 benzacridines (2 series). It was found that the proposed relation could not discriminate between carcinogenically active and inactive compounds. Thus, the two carcinogenic 1,2,5,6- and 1,2,3,4-benzophenanthrenes had J₁ values (1380 and 1200) which were lower than 2/3 inactive derivatives (3,7,8- and 2,3,5,6-dibenzophenanthrene; values 200 and 2100). The author prefers the "K-L regions" theory of carcinogenesis, which not only distinguishes between active and inactive compounds, but also accounts for their relative efficiencies. The simplest hypothesis for the mechanism of action of the chemical carcinogens (for the related mutagens) is, that a damage is produced in a protein involved in growth control, or directly in a nucleic acid, by a chemical interaction.

422 CODING OF BACTERIAL NUCLEIC ACID WITH ALKYLATING AGENTS. (E., Abstract) Lorán, M. J. (Dept. Int. Med., Washington U., St. Louis) and W. J. Harrington. *Clin. Res.* 1(2):232, 1963.

Addition of triethylene melamine at 50 µg/ml to the growth medium of wild type *Escherichia coli* did not inhibit replication of the bacteria, but the alkylated cells were abnormally large. Of 72 clones isolated, 5 showed new antigenic genotypes each with distinct specificities against rabbit antisera tested directly and following cross absorption. The new antigens were demonstrable only in the soluble fraction of disrupted cells and only in the alkylated population. The data support the concept that alkylating agents induce, at random, mutants with new antigenic specificities.

63-423 INTERACTION OF INSULIN AND CHLORPROMAZINE IN TERATOGENESIS. (E.) Landauer, W. (Dept. Anim. Genetics, U. Connecticut, Storrs) and E. M. Clark. *Nature (London)* 198:215-216, 1963.

In 4-5-day-old White Leghorn chick embryos, inj. of chlorpromazine (2.5 mg/egg) plus 2 or 4 units of insulin doubled the frequency of micromelia and beak defects over that observed in embryos receiving insulin alone. Chlorpromazine alone caused few abnormalities, without significant effect on embryo mortality in 1/2 experiments. There was a significant increase in embryo mortality (especially of embryos aged 7-13 days), when chicks were inj. with both agents. Results are in agreement with the hypothesis that the teratogenic effect of insulin in 4-5 day embryos is due to uncoupling of oxidation phosphorylation.

63-424 IMMUNOLOGICAL INTERRELATIONS IN RATS WITH DOUBLE TUMORS (MC SARCOMA AND DAB HEPATOMA). (Jap.) Tsuji, Y. (Dept. Path., Res. Inst. Cancer Immunol., Hokkaido U., Japan). *Gan no Rinsho (Jap. J. Cancer Clin.)* 8(10):644-649, 1962.

Rats transplanted repeatedly by one of a pair of double tumors (20-methylcholanthrene (20-Me) induced ascites sarcoma and dimethylaminoazo-benzene (DAB) induced hepatoma) completely inhibited the homologous tumor and showed anti-transplantability against the heterologous tumor. Thus specific anti-transplantability between them was not shown. Immunization with the TCA fraction of normal organs in rats with double tumors did not produce anti-transplantation immunity. In rats immunized by each of the double tumors, only the 20-Me immunized group showed strong anti-transplantation immunity against Usubuchi sarcoma (ascites type) and Takeda sarcoma (ascites type) while DAB immunized mice showed anti-transplantation immunity against GDT2 hepatoma (ascites type). Specific immunity between them was still observed but only very weakly. Insoluble lipid protein (TCA fraction) of each tumor also did not show specific anti-transplantability.

63-425 CANCEROUS DEGENERATION OF LARYNGEAL WARTS (HYPERKERATOTIC PAPILLOMAS). (It.) Berlendis, P. A. (Clin. Oto-Rhino-Laryng., U. Pavia,

Italy). Boll. Soc. Medicochir. Pavia 76(1-2):33-43, 1962.

Two cases of laryngeal wart, usually considered a precancerous condition, are reported, one in a 51-year-old man, the other in a 38-year-old man. Both were smokers (20 and 25-30 cigarettes a day for 30 and 20 yr., resp.), and both presented with dysphonia of 3 and 1 yr. duration, resp. Both were treated successfully by surgery. Almost all cases of laryngeal warts originate in the vocal cords; major importance is ascribed to chronic laryngitis. Laryngeal warts are to be classified in Aschoff's second group of precancerous conditions: hyperplastic forms involving tissue proliferation caused by various types of irritant stimuli-cigarette smoke in these 2 cases.

63-426 20-METHYLCHOLANTHRENE INDUCED SURFACE TUMOURS IN MICE AND THEIR TRANS-PLANTATION. (E.) Reddy, D. J. (Dept. Path., Andhra Med. Coll., Visakhapatnam, India), P. Syamasundara Rao and B. Maharaja Saran. J. Indian Med. Prof. 9(10):4375-4377, 1963.

Application of a 0.6% soln. of 20-methylcholanthrene in acetone to the skin of 13 male Swiss mice produced multiple papillomas progressing to epitheliomas, and in 1 case to secondary tumors in the lung. Among 17 mice given s.c. inj. of a 1% suspension of the carcinogen in olive oil, 3 developed histologically confirmed fibrosarcomas. A technic is described which enabled the authors to transplant these fibrosarcomas s.c. to recipient mice over 4 tumor generations.

63-427 THE MALIGNANT MELANOMA OF HAMSTERS: III. EFFECTS OF SEX AND CASTRATION ON THE GROWTH OF THE TRANSPLANTED TUMOR. (E.) Rosenberg, J. C. (U. S. PHS Hosp., Staten Is., N. Y.), C. Assimacopoulos and S. A. Rosenberg. Ann. N. Y. Acad. Sci. 100(Pt. 1):297-304, 1963.

Pooled tumor tissue of the Fortner melanoma (0.2 ml of a 50% suspension in 0.9% saline), was inj. into the inguinal region of 48 male and female hamsters, 5-10 mo. old, mean wt. 114 g and 137 g, resp. Growth characters of the resulting tumors studied in detail for over a mo. showed mean tumor volume in 12 females to be consistently greater than in 11 males. Tumor take showed no difference between orchiectomized (22) and sham operated controls (21); but the latent period was shorter in those that were castrated (77% with measurable tumors at 17 days compared to 43% in controls). Tumor growth rates were similar in both, but due to an early growth lag in the controls, the growth curve for the orchiectomized animals remained consistently higher. Mean body wt. of orchiectomized hamsters also increased (about 10%), apart from tumor growth. Growth rates were likewise similar in normal and in oophorectomized females, and their tumor takes were alike; but the tumor size in

normal females was significantly and consistently higher than in oophorectomized hamsters (tumor volume at 29 days, 5.8 ml and 2.9 ml, resp.).

63-428 EFFECT OF FATTY ACIDS ON CARCINO-GENESIS. (Ger., Abstract) Schramm, T. Wiss. Zschr. Humboldt-Univ. Berlin (Math. Naturw. Reihe) 11(1):184-185, 1962.

Ethylesters of stearic, oleic, linoleic and linolenic acids were given p.o. or intra-gastrically to mice and rats. Linolenic acid completely inhibited the formation of liver cancer in animals fed 3'-methyl-4-dimethylaminoazobenzene (controls showed about 50% incidence); in animals fed 4-dimethylaminostilbene, it decreased the incidence of squamous cell carcinoma of the external auditory canal from 78% to 14%; in those receiving 2-acetylaminofluorene, linolenic acid diminished the incidence of cirrhosis of the liver, and tumor incidence was somewhat decreased. However, it did not inhibit carcinogenesis in animals receiving 20-methylcholanthrene, 9,10-dimethyl-1,2-benzanthracene or the ethyl ester of carbamic acid. The growth of transplanted Walker carcinoma in rats was not affected by linolenic acid. The fact, that the cancer inhibitory effect of linolenic acid was limited to carcinogenic substances which induce liver cancer, while effect of other carcinogens and the growth of transplantable tumors were not influenced, is ascribed to the special role of the liver in fat metabolism and the detoxification of carcinogenic and other foreign substances.

63-429 THE HEMOPOIETIC TISSUE TOXICITY OF BENZENE VAPORS. (E.) Deichmann, W. B. (Dept. Pharmacol., U. Miami Sch. Med., Coral Gables, Fla.), W. E. MacDonald and E. Bernal. Toxic. Appl. Pharmacol. 5(2):201-224, 1963.

Exposure of rats to benzene vapor at av. conc. of 831, 65 or 61 ppm in air for 5 hr./day on 4 days/week resulted in significant leukopenia in 2-4 weeks, while 44-47 ppm yielded moderate leukopenia in 5-8 weeks and lower conc. had no effect, even in 3-7 mo.; there was no change in RBC or Hb in any of the rats. Hexane was found to be non-toxic. Autopsies on some of the leukopenic rats showed only chronic bronchopneumonia (also found in controls) and splenic hemosiderosis

63-430 ACIDIC POLYSACCHARIDES IN CANCER. (E.) Takeuchi, M. (Kurume U. Sch. Med., Kyushu, Japan) and Y. Tanaka. Kurume Med. J. 10(1):37-50, 1963.

After p.o. feeding of p-dimethylaminoazobenzene to male Wistar rats for 30, 60, 90 or 120 days before sacrifice, the neutral polysaccharides of the liver, derived from glycoprotein, generally decreased throughout the period of the experiment but showed increases at 1 and 4 mo., corresponding to the periods of acute inflammation and

cancerization, resp. The hyaluronic acid and chondroitin sulfate gradually increased, paralleling an increase in collagen protein, while heparin was unchanged. There were also increases in incorporation of radioactive sulfate, the S^{35} /uronic acid ratio, and the macromolecular fraction of the mucopolysaccharides, while the macromolecular fraction decreased. Studies in cancer pts. showed generally similar results, but a comparison of gastric carcinomas (1 ulcerative and 1 proliferative), showed a low polysaccharide content compared to hyaluronic acid and chondroitin sulfate in the former and a high polysaccharide content in the latter. Similar differences were observed between primary and metastatic hepatic carcinoma, the primary tumor showing mostly polysaccharide and hyaluronic acid while metastases from mammary carcinoma showed more hyaluronic acid and chondroitin sulfate. Compared to normal subjects, pts. with cancer showed a marked change in distribution of serum proteins and polysaccharides; whereas, in the normal, fraction I contained 64.54% of the protein and 92.64% of the polysaccharide, the corresponding figures were 32% and 88.69% in cancer of the stomach and 15.76% and 20.06% in uterine cancer, the marked increases being in fractions 2,3 and 4 for proteins and 4,5 and 6 for polysaccharides.

431 STUDIES ON LEUKEMIA IN THE C3Hf STRAIN OF MICE. I. ORIGIN, TRANSMISSION, AND MORPHOLOGY OF SPONTANEOUS LYMPHATIC LEUKEMIA. (J.) Miyoshi, I. (Dept. Int. Med., Okayama U. Med. Sch., Japan). Acad. Med. Okayama 16(4): 33-302, 1962.

Lymphatic leukemia was found in 1/3 C3Hf/Bi/K1 mice, implanted intraocularly 3 mo. previously with a 20-methylcholanthrene-induced ascitic lymphoma. This new C3Hf leukemia was transmitted to over 80 C3Hf adult mice by i.p. inoc. of minced tumor fragments, lymphoid tumor emulsions, or ascitic lymphoma cells, and carried through 20 generations by successive tail grafts, with 100% successful grafts, with constantly increasing virulence, and more rapid tumor growth. After s.c. inoc. leukemia developed, but without ascites. Attempts to transplant this leukemia into other strains (including DBA) failed. The gross and microscopic descriptions given, including blood picture, fulfill the criteria for a lymphoid neoplasm of mice. The failure to infect DBA mice, absence of neoplastic growth at the original ocular implantation site, and failure to isolate a filterable virus from DBA leukemia, support the conclusion that this is a spontaneous, strain-specific leukemia.

432 A STUDY OF THE CARCINOGENIC PROPERTIES OF TOBACCO TAR. (Ger.) Seelkopf, C. (German Res. Inst. for Food Chem., Munich), Ricken and G. Dhom. Zschr. Krebsforsch. 63(3):241-249, 1963.

Equal numbers of male and female, 2 month-old, brother-sister-mated BDT rats were treated with fractions or residuals of cigarette smoke tar, as follows: (A) residuals after fractionation (neutral), 12.5-50 mg/100 g body wt., s.c. in olive oil at 14-day intervals to a total of 730-878 mg; (B) "Fraction I" (neutral), 12.5-25.0 mg/100 g, s.c. in olive oil at 8-day intervals to a total of 795-990 mg; (C) "Fraction II" (neutral), 25-50 mg/100 g, s.c. in olive oil at 8-day intervals to a total of 435-510 mg; (D) "Fraction III" (acid), 12.5-50 mg/100 g, s.c. in aqueous soln. at 8-day intervals to a total of 750-920 mg; (E) "Fraction IV" (nicotine-free base), 12.5 mg/100 g, s.c. in 1,2-propylene glycol at 8 day intervals to a total of 291-341 mg; (F) "Fraction V" (a weak base), 6.25-12.5 mg/100 g, s.c. in 1,2-propylene glycol at 8-day intervals to a total of 197-230 mg. At the end of 1 yr. or more, total tumor incidence was tabulated as follows: controls receiving only propylene glycol, approx. 4% (fibromas); controls receiving only olive oil, approx. 8% (fibromas); (A), 46% (fibromas, differentiated and undifferentiated sarcomas, and leukemia); (B), 15% (fibromas, undifferentiated sarcomas, and carcinomas); (C), 19.1% (fibromas, differentiated and undifferentiated sarcomas, and carcinomas); (D), approx. 15% (all 5 types of tumors); (E), approx. 15% (fibromas, undifferentiated sarcomas, carcinomas, and leukemia); (F), approx. 6% (fibromas, carcinomas). Among 7 tumors not occurring at the site of inj. (all genital tumors in females), demonstrable deposits of tobacco tar were found in 2.

63-433 OBSERVATIONS ON SUBCUTANEOUS AND INTRAMUSCULAR METHYLCHOLANTHRENE TUMORS IN THE RAT. (Ger.) Betzler, H. J. (U. Clin., Eberhard-Carls U., Tuebingen, Germany). Zschr. Krebsforsch. 65(3):252-253, 1963.

Single s.c. or i.m. inj. of 20-methylcholanthrene (0.5-2% in olive oil, 5-20 mg) resulted in tumors in 48/49 rats. The 33 s.c. and 28 i.m. sarcomas obtained included 31 spindle cell, 18 spindle cell polymorphocellular, 3 polymorphocellular, 3 reticular and 6 undifferentiated sarcomas, there being no significant difference between s.c. and i.m. tumors in the distribution of histological types. The i.m. sarcomas did, however, show a greater tendency to spread to adjacent tissues.

63-434 PROTOPORPHYRIN, CIRRHOSIS AND HEPATOMATA IN THE LIVERS OF MICE GIVEN GRISEOFULVIN. (E.) Hurst, E. W. (Imp. Chem. Indust. Ltd., Macclesfield, Cheshire, England) and G. E. Paget. Brit. J. Derm. 75(3):105-112, 1963.

Random-bred male and female mice fed diets containing 0.5-2.5% griseofulvin (G) for periods of as long as 435 days generally showed few ill effects, but their livers gradually changed color and increased in size as the result of marked hypertrophy and the deposition of protoporphyrin in the liver cells and biliary tract; this

derangement in porphyrin metabolism resulted in intrahepatic biliary cirrhosis and perilobular fibrosis due to the proliferation of small bile ducts. Ultimately, the combination of a chronic derangement in structure and a continual stimulus to cell proliferation resulted in a high incidence of hepatomas, multiple lesions being found at 435 days in 10/13 fed 1% G and 5/20 fed 0.5% G. Some strains of mice, particularly B.S.V.S., also showed increased susceptibility to infection. In general, admin. of G by stomach tube as a single 100 mg dose per day had little effect on the liver, but the typical effects were again produced if the dose was divided into 9 hourly doses, indicating that continuous presence of the agent is required; the type of diet admin. had no effect. Although after i.p. admin. there were some changes in the liver, s.c. inj. was ineffective. Comparable hepatic changes could not be observed in rats, guinea pigs or rabbits fed comparable doses of G.

- 63-435 CHANGES IN CELLULAR DEOXYRIBONUCLEIC ACID IN MOUSE SKIN FOLLOWING APPLICATION OF A TUMOUR-PROMOTING AGENT. (E.) Meek, E. S. (Dept. Path., U. Bristol, Gr. Brit.). Exp. Cell Res. 29(3):389-393, 1963.

Absorptiometric measurements of Feulgen-stained epithelial nuclei showed that the cellular proliferation (thickening of the epidermis and an increased mitotic rate) appearing in the dorsal skin in response to painting with neat Sweet Orange Oil (0.1 ml on days 1, 3, 5, 8, 10 and 12) in adult male mice sacrificed on day 15 was accompanied by a 21% increase in the number with DNA complements greater than diploid (up to tetraploid), but no alteration in the stem-line value. This is consistent with simple hyperplasia of a normal tissue.

- 63-436 INDUCTION OF PULMONARY TUMORS IN C57BL MICE USING STRINGS IMPREGNATED WITH 20-METHYLCHOLANTHRENE. (E.) Stevenson, J. L. (Dept. Path., Ohio State U., Columbus) and E. von Haam. Acta Cytol. (Phila.) 7(2):126-128, 1963.

The insertion of cotton or silk threads impregnated with 20-methylcholanthrene (approx. 0.8 mg per thread) into the lungs of male C57BL mice, which were sacrificed after 8-12 mo., resulted in the appearance of 40 pulmonary tumors in 47 animals, including 26 spindle cell sarcomas, mostly arising from the chest wall, 3 adenocarcinomas arising in the peripheral areas of the lung, 6 squamous cell carcinomas arising within the lung parenchyma, 1 carcinoma *in situ*, 4 lymphosarcomas and 1 adenoma; all the carcinomas appeared from 4-6 mo. after implantation of the threads. The only difference between the cotton and silk threads was that the former apparently absorbed the carcinogen more uniformly, resulting in a higher incidence of carcinomas (31%) than with the silk thread (7.1%). The

incidence of sarcomas was 78.6% and 58.0% in animals receiving silk and cotton threads, resp.

- 63-437 THE CONTENTS OF 3,4-BENZOPYRENE IN SMOKED SPRAT AND SMOKE IN VARIOUS SMOKING METHODS. (Rus.) Gorelova, N. D. (Exp. Oncol. Lab., Inst. Oncol., Acad. Med. Sci., Leningrad), P. P. Dikun, O. P. Gretskaia and A. V. Emshanova. Vop. Onkol. 9(3):53-58, 1963.

In the preparation of smoked sprats, under conditions of high smoke temperature, the av. 3,4-benzpyrene (BP) content ($\mu\text{g/kg}$ of fish) was 8.5 with wood, 1.8 with sawdust, 34 with chips (in mechanized stove), 58.3 with wood and 3.1 with sawdust (in electrostatic field). In smoking at a lower temperature, using a mechanized stove, values for sawdust and wood were 0.8 and 163, resp.; a combination of both was 1.0. Aspen wood with a smoke temperature of 680-780°C, gave BP values of 5-103 $\mu\text{g/cubic meter (m}^3\text{)}$ of smoke, alder wood in experimental stove (NIIMRP), at 555-750°C, had 26-57 $\mu\text{g/m}^3$; smoke of various types of sawdust, at 450-480°C contained 0-1.1 $\mu\text{g/m}^3$. Analyses of wood and sawdust smoke for other ingredients gave these values (mg/m^3), resp.: tar, 2540 and 320; phenols, 200 and 13; volatile acids, 1,000 and 54; neutral compounds, 140 and 24; ether insoluble compounds 630 and 173; aldehydes, 108 and 1; ketones, 1 and 1; BP, 0.048 and 0.0007.

- 63-438 THE EFFECT OF SYNESTROL ON THE UTERUS OF CASTRATED AND NON-CASTRATED RATS. (Rus.) Charkviani, L. I. (Inst. Oncol., Acad. Med. Sci. USSR, Moscow). Akush. Ginek. 38(3):41-45, 1962.

Admin. of hexestrol (synestrol; 0.1 ml 2% soln. s.c. every 5 days) to 96 8-week-old female rats, 47 of which had been castrated at the age of 4-5 weeks, resulted in enlargement of the pituitary, hepatic hyperemia and cornification of the vaginal epithelium, as well as a series of uterine changes which were most pronounced in the castrated group. Catarrhal-desquamative and purulent-necrotic inflammation and fibrosis of the uterus appeared in 34 castrated and 37 intact rats after 2-3 mo. of treatment; after 10-12 mo., some of each group showed replacement of the cylinder-cell epithelium by squamous epithelium and papillomatous foci in the uterine wall. Neoplastic changes appeared only in 2 castrated (papillomas undergoing malignant degeneration) and 2 non-castrated (1 with adenocarcinoma and 1 with a large adenomatous polyp) rats. Controls outlived treated animals, and showed no significant uterine changes, except that castration led to uterine atrophy.

- 63-439 A GENETIC STUDY OF INDUCED LUNG-TUMOURS IN MICE. (E.) Falconer, D. S. (Inst. Animal Genet., Edinburgh, Scotland) and J. L. Bloom. Brit. J. Cancer 16(4):665-685, 1962.

The heritability of susceptibility in random-bred JC and LX mice of both sexes to lung tumor induction by urethan was determined by the resemblance between parents and their similarly urethan-treated offspring with respect to number of tumors induced, as compared with the same data for six inbred strains and crosses. The variation within each strain was apportioned to genetic and non-genetic causes by multifactorial inheritance methods of statistical analysis. It was concluded that the most important cause of the wide differences in susceptibility among the individuals of both strains (mean tumors, 3.42 and 8.19; variances, 5.50 and 51.92, resp.) was genetic to the extent of 80%-90%. Environmental factors accounted for almost 11% of the total variance of tumor number. The wide range of genetic diversity in susceptibility to tumor induction is not confined to differences between inbred strains, but exists equally among the individuals of random-bred strains which are the laboratory equivalent of a natural population.

440 THE INFLUENCE OF CROTON OIL STIMULATION ON TUMOUR INITIATION BY URETHANE IN MICE. (E.) Pound, A. W. (Brisbane Hosp., Australia) and J. R. Bell. Brit. J. Cancer (4):690-695, 1962.

Twenty groups of 20 male mice each were inj. s.c. with 25 mg of urethan in 0.5 ml of isotonic saline. The skins of 19 of these groups were also painted once with croton oil (0.5% in acetone, 0.25 ml) 13, 8, 7, 6, 5, 4, 3, 2 days, 18, 12, and 6 hr. before, at the same time, and 6, 12, 18, 24 hr., and 2 or 3 days after the urethan inj. For 20 weeks thereafter, the groups plus a control group were painted weekly with croton oil. In the controls, no other agent alone induced any tumor. In the test groups, the number of mice with tumors varied from 1 to 8 in 16/19, but in the 3/19 groups painted with croton oil 18, 24, and 48 hr. before the urethan inj., there were 26, 39 and 24 papillomas, in 11/13, 10/15, and 9/14 survivors, resp.; time to the appearance of the first tumor was shorter (6 weeks) compared to the other groups (6-10 weeks).

441 THE LOCALISATION OF THE INFLUENCE OF CROTON OIL STIMULATION ON TUMOUR INITIATION BY URETHANE IN MICE. (E.) Pound, A. W. (Brisbane Hosp., Australia). Aust. J. Biol. Med. Sci. 41(Pt. 1):73-80, 1963.

Eighty Hall mice, in 6 groups of 20 each, were inj. s.c. in the interscapular region with 25 mg of urethan (U); five of the six groups were painted 18 hr. previously with 0.25 ml of croton oil (0.5% in acetone); group 2 over all the back, groups 3-6 on $\frac{1}{2}$ the skin of the back (right or left side, fore or rear half). Starting 7 days after the U inj., the croton oil paintings of the

whole back were repeated weekly for 20 weeks. At 22 weeks, of the 59 survivors in groups 3-6, 25 mice had no tumor; 16 had tumors (papillomata) on both the halves that received the preliminary paintings and those that were unpainted, 16 had tumors only on the painted half, and 2 on the unpainted half only. In the same groups, there were a total of 58 tumors on the skin halves given the preliminary painting with croton oil, 20 on the other halves. In 6 unpainted mice, there were 9 tumors; there were 32 tumors in 10 mice painted over the entire back. This pattern in the augmenting effect of preliminary painting with croton oil on the initiation of tumor formation by U indicates that it is due to local changes produced in the skin by the croton oil, and not to a general metabolic effect.

63-442 CHOLESTEROL AS CARCINOGEN. I. SARCOMA INDUCTION BY CHOLESTEROL IN A SENSITIVE STRAIN OF MICE. II. CROTON OIL A COMPLETE CARCINOGEN. (E.) Hieger, I. (Roy. Cancer Hosp., London). Brit. J. Cancer 16(4):716-721, 1962.

In mice of the C57, C57 x C3H, Swiss S, BALB/C, and stock (random-bred) strains, three s.c. inj. of 0.2 ml of a 9% suspension of pure or commercial cholesterol in olive oil induced in some mice, up to 5% sarcomas at the inj. site. The incidence of sarcomas sometimes could be increased by enlarging the dose (5 inj. of 0.3 ml each); by giving the first inj. to day-old mice; by substituting lard for the olive oil; by adding egg powder to the diet; or by crowding the mice. Mice of the Buffalo and BRO strains were especially sensitive: after inj. of commercial cholesterol, 16/50 Buffalo mice developed sarcomas, and 38/50 lived more than a year. Addition of croton oil to the cholesterol also increased sarcoma production. Croton oil alone (0.4% in olive oil, 0.2 ml x 3) produced sarcomas in 4/35 BRO mice. It is concluded that susceptibility to carcinogenesis, by cholesterol or by croton oil, is determined largely by the genetic constitution of the mouse. Within pure-bred-strain differences may be due to slight residual genetic differences in apparently isogenic strains; or, diet in early life may modify susceptibility. It is also concluded that croton oil is in itself a complete carcinogen.

63-443 THE EFFECTS OF TUMOUR INITIATING AGENTS ON MOUSE SKIN SULPHYDRYL LEVELS. (E.) Calcutt, G. (Mount Vernon Hosp. Radium Inst., Northwood, Middlesex, England) and D. Doxey. Brit. J. Cancer 16(4):806-810, 1962.

Tissue sulphydryl (-SH) groups of Strong A mouse skin (total, TCA-soluble, and protein bound) were measured at intervals from 15 minutes to 24 hr. after single doses of 7 agents with known initiating activity (1,2-benzanthracene, β -propiolactone, 3,4-benzpyrene, 9,10-dimethyl-

1,2-benzanthracene, urethan, chlorambucil and TEM) and 9 related non-carcinogenic compounds. All agents showed the same general pattern of results: a transient rise in total -SH levels between 15 minutes and 3 hr. followed by a slight fall below the mean control value and a gradual return to near the normal level. TCA-soluble and protein bound -SH values ran approximately parallel to the total figures. In all the agents tested, the TCA-soluble -SH values fell to zero (or below a detectable level) at some time during the 24 hr. In their effects on -SH level, no difference could be found between tumor-initiating agents and their inactive related compounds. The results suggest that tumor-initiating agents do not act by direct inhibition of tissue sulphhydryl groups. However, reaction with a limited number of cellular -SH groups could occur without affecting the measurable levels.

63-444 DEMONSTRATION OF AN ANTIGENIC FACTOR SPECIFIC IN CANCERIZATION. (Fr.)

Dufour, D. (Fac. Med., U. Laval, Quebec, Canada). *Rev. Franc. Etud. Clin. Biol.* 8(2):171-172, 1963.

Adult male Sprague-Dawley rats (50) were divided into 3 groups receiving (a) a normal basic, synthetic diet, (b) the basic diet + 4-dimethyl-aminoazobenzene (DAB), and (c) the basic diet + 4-diethylaminoazobenzene, a non-carcinogenic compound. After 2 mo. at weekly intervals, 3 rats/group were killed and their livers were examined for the appearance of soluble antigens to serum from a rabbit previously inj. with Walker tumor. Three mo. after initiation of the experiment the livers of DAB fed rats, but not the controls, showed an antigen identical to that found in rats with Walker tumor. The identity of the factor was checked both by double gel diffusions and by immunoelectrophoresis.

63-445 TERATOGENIC INTERACTION OF INSULIN AND 2-DEOXY-D-GLUCOSE IN CHICK DEVELOPMENT. (E.) Landauer, W. (Storrs Agric. Exp. Stat., U. Connecticut) and E. M. Clark. *J. Exp. Zool.* 151(3):245-252, 1962.

Eggs of White Leghorn fowl were inj. at 96 hr. of incubation with 2-deoxy-D-glucose (2-DG; 0.25, 0.5, or 0.6 mg/egg) and the number of embryos surviving the 13th day, resp., was 251/266, 196/262, and 173/265; rumplessness occurred in 1.2%, 4.1%, and 6.4%, resp.; micromelia, in 0.4%, 0%, and 0.6%, resp.; miscellaneous defects, in 1.2%, 2.0%, and 2.9%, resp. Toxic doses of 2-DG (0.75 mg/egg) were overcome by supplementary glucose (10 mg/egg). Admin. of 1 U insulin plus 2-DG, 0.5 or 0.6 mg/egg at the 96-hr. stage, resulted in significant potentiation of teratogenic effects (micromelia, 16.3, 24.7%; beak defects, 11.3, 10.1%; bupthalmia, 3.8, 7.9%; with 1 U insulin alone, results were, resp., 5.4%; 2.7%; and 0%).

Combined with 1 U of insulin, 0.1 mg of 2-DG at the 24-hr. stage produced a highly significant rise in the incidence of rumplessness as well as occurrence of tibio-tarsal joint abnormalities. Admin. of 1 U of insulin alone, or of 1 U of insulin plus 0.1 mg of 2-DG, or of 2-DG alone (0.1 mg and 0.2 mg), resulted, resp., in 121/210, 106/407, 100/166, and 85/164 survivors on day 13; in rumplessness, 39.7%, 66.5%, 5.0%, and 7.1%, resp.; in malformations of the tibio-tarsal joint, tarsometatarsus and toes in 0%, 7.5%, 0% and 0%, resp.; insulin, 2 U, supplemented with glucose, 5 or 10 mg, inj. at the 24-hr. stage, resulted, resp., in 115/167 or 124/162 survivors on day 13, and 44.3% or 35.5%, rumpless as compared to 92/165 survivors and 42.4% rumpless in eggs treated with 2 U of insulin alone. At 96 hr. of incubation, 2 U of insulin plus 5 mg glucose resulted in 82/104 survivors on day 13, 31.7% micromelia, and 8.5% abnormal beak, as compared to 80/119, 37.5%, and 5.0%, resp., with 2 U of insulin alone. It was concluded that the 2-DG alone was not teratogenic at either of the 2 developmental stages; that its toxicity could be overcome by supplementary glucose; and that the synergism of 2-DG and insulin and the teratogenic activity of insulin itself are clearly intracellular events. Glucosamine, β -hydroxybutyric acid, galactose, and N-acetylglucosamine had no effect on the teratogenic activity of insulin, while 2-DG potentiates the effects of 6-aminonicotinamide and of pilocarpine in a manner similar to insulin; no potentiating effects of 2-DG were encountered in combination with 3-acetylpyridine, eserine, or sulfanilamide.

63-446 THE INTERACTION IN TERATOGENIC ACTIVITY OF THE TWO NIACIN ANALOGS 3-ACETYL-PYRIDINE AND 6-AMINONICOTINAMIDE. (E.) Landauer, W. (Storrs Agric. Exp. Stat., U. Connecticut) and E. M. Clark. *J. Exp. Zool.* 151(3):253-258, 1962.

Eggs of White Leghorn fowl were inj. at 96 hr. of incubation with 6-aminonicotinamide (6-AN), and/or 3-acetylpyridine (3-AP) and the incidence of micromelia, muscular hypotrophy, short upper beak, and miscellaneous defects were noted in survivors on day 13. Effects observed were in good accord with an earlier report. The characteristic teratological consequences of 6-AN could be completely or nearly completely prevented by an 86-200-fold supplementation (wt./wt.) with 3-AP. However, the characteristic teratological consequences of treatment with 3-AP (muscular hypoplasia) was exaggerated when 2.5-5 μ g of 6-AN were added to either 375 or 500 μ g of 3-AP. The teratogenic exacerbations were exaggerated in both incidence and degree of expression. The beneficial results of 3-AP on 6-AN teratogenicity, and the exacerbation of 3-AP teratogenicity by 6-AN were discussed, resp., in terms of the ability of 3-AP pyridine nucleotide and the inability of 6-AN pyridine nucleotide in taking over some of the metabolic functions of nicotinamide adenine dinucleotide. (See also preceding abstract.)

- 63-447 A UNIFIED CONCEPT OF CANCEROGENESIS. (E.) Fiala, S. (Dept. Path., Columbia U., New York) and W. Glinsmann. Neoplasma (Bratisl.) 10(1):83-96, 1963.

A concept is submitted to account for the mechanism of carcinogenesis. Its main points are: the cells within a metazoan organism which get freed of their functional and structural bonds to the organism, are malignant. These bonds are ascribed to the adaptive enzyme system of the cell with the structural basis in the cytoplasm. Cancerogens are agents, chemical or biological (viruses), which persistently interfere with the function of this system until, at mitosis, the conditions for the replication of the structural counterpart of the interfered-with adaptive system are not met. In distinction to the parent cell which is carcinogen-containing and organism-dependent, the daughter cell is cancerogen-free but organism-dependent. Tumor cells, consequently, do not contain either carcinogens or oncogenic viruses. The maintenance of the intact adaptive enzyme system depends thus on the circulation of information between the cytoplasm and the nucleus. In carcinogenesis it is this "memory" which may be lost after the removal of the cell from the organism, or by interference with the messages from the cytoplasm due to the metabolism of the cancerogen and/or its binding by the structural network of the ergastoplasm.

- 63-448 EFFECT OF SOME SUPPLEMENTARY FACTORS ON THE DEVELOPMENT OF THE EXPERIMENTAL SKIN CANCER. (Rus.) Solomina, V. F. (Inst. Clin. Exp. Surg., Acad. Sci. Kaz. SSR). Tr. Inst. Klin. i Eksp. Khir., Akad. Nauk Kaz. SSR 8:121-127, 1962.

Of 114 mature white mice, 21 (A; controls) received 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.25% in oil, 1 drop every 3-4 days for 4 mo. in the interscapular region); 36, B, DMBA as above and lead acetate (0.1% aqueous solution, 0.2 ml every 5 days for 4 mo. by gastric intubation); 24, C, DMBA as above and dust suspension containing 98.77% of silica (single, intratracheal admin., 5-10 mg in saline); 33, D, DMBA as above and to the same region P^{32} (0.1 μ Ci, 100-150 cpm every 15 days for 4 mo.). Animals were sacrificed after 15 days, 1, 1½, 3, 6 mo. Macroscopic observation showed: after 1 mo. in A-D alopecia; after 3 mo. in A single papillomas, B and C papillomas, D papillomas and tumors; after 3½-4 mo. in A-C papillomas, in B papillomas and tumors; after 5 mo. in A, B papillomas, B, C and D, papillomas and tumors; after 6 mo. in A, papillomas, B and C tumors, tumor and papillomas. Microscopically, after 1 mo. all groups showed skin hyperplasia; carcinoma already appeared in group D. After 3 mo. cancer appeared in groups C and D, after 6 mo. in all groups but A and after 5 mo. in 1 groups. Silicon was determined histologically

and lungs had the appearance of lymphangitis, perivascularitis, panbronchitis with large macrophage cell reaction and with formation of silicon nodes in the initial stage. The results showed that the precancerous period was shortened with P^{32} to 3 mo., with lead acetate to 3½ mo. and with silica to 4 mo.

- 63-449 THE INTERACTION OF THE CARCINOGEN N-METHYL-N-NITROSOURETHANE WITH CYSTEINE IN VITRO. (E., Abstract) Schoental, R. (Med. Res. Council Lab., Carshalton, Surrey, England) and D. J. Rive. Biochem. J. 87(2): 22P-23P, 1963.

The in vitro reaction between N-methyl-N-nitrosourea (NMU) and cysteine at room temperature and physiological pH was studied and the products of this reaction analysed. By one-dimensional paper chromatography (in a butanol acetic acid:water solvent system), 2/3 of the main ninhydrin-positive spots were carbonyl-containing compounds. A 4th ninhydrin-negative spot was resolved by two-dimensional chromatography into 5 spots, 4 of which were ninhydrin-negative spots which contained carbonyl-containing compounds. The primary reaction between NMU and -SH compounds appears to be the addition of the latter to the carbonyl group of NMU followed by release of nitrogen and a methylene radical. The latter then methylates any free sulfhydryl or carboxylic groups.

- 63-450 RATE OF METABOLISM OF 9,10-DIMETHYL-1,2-BENZANTHRACENE IN NEWBORN AND ADULT MICE. (E.) Domskey, I. I. (Div. Oncol., Chicago Med. Sch., Illinois), W. Lijinsky, K. Spencer and P. Shubik. Proc. Soc. Exp. Biol. Med. 113(1):110-112, 1963.

After admin. of 9,10-dimethyl-1,2-benzanthracene (DMBA; 3% in olive oil, 0.1 ml, i.p.) to adult Swiss mice, 10% of the inj. dose was present after 4 days. In newborn mice (17-24 hr. old) after i.p. admin. of 0.16 mg DMBA in olive oil, 10% of the inj. dose was present 10 days later. The quantity of DMBA in the adult carcass rose to 200-250 μ g within 1 hr., remaining constant thereafter, whereas DMBA in the peritoneal cavity declined exponentially. The greater susceptibility of newborn mice to DMBA tumor induction is believed to be due to the longer persistence of the compound in the newborn.

- 63-451 NUCLEOLAR "CAPS" - A MORPHOLOGIC ENTITY PRODUCED BY THE CARCINOGEN 4-NITROQUINOLINE N-OXIDE. (E.) Reynolds, R. C. (Dept. Path., U. Texas Southwestern Med. Sch., Dallas), P. O'B. Montgomery and D. H. Karney. Cancer Res. 23(4):535-538, 1963.

Distinctive morphological changes produced by 10^{-3} to 10^{-6} M soln. of 4-nitroquinoline N-oxide in Chang liver cells were demonstrated by means of

histological stains, electron microscopy, and time lapse motion picture studies of living cells under the phase-contrast microscope. The principle changes included: nuclear exhaustion manifested by reduction in size; fusion of nucleoli; separation of the pars amorpha and nucleolonema to produce 2 types of nucleolar "caps". With electron microscopy, dark nucleolar "caps" of marginated electron dense particles were present; in some cases, a light nucleolar "cap" was also seen. One of these 2 types of "caps" was present in over 50% of cells surviving treatment. "Caps" formed in treated living cells and were seen in cells fixed with potassium permanganate prior to treatment. Nuclear heterochromatin condensed about areas of the nucleoplasm producing a vacuolated appearance as evidenced by electron and fluorescence microscopy. The vacuoles are believed to contain ribonucleoprotein. A loss of cytoplasmic basophilia was observed. The author speculates that the morphological changes represent the cell's response to decreased cellular protein synthesis.

- 63-452 EFFECT OF CARCINOGENIC POLYNUCLEAR HYDROCARBONS ON THE METABOLISM OF OESTROGENS. (E.) Jellinck, P. H. (Cancer Res. Centr., U. British Columbia, Vancouver, Canada) and L. Irwin. Nature (London) 198:787-788, 1963.

Liver microsomes of 40-50-day-old female Sprague-Dawley or Wistar rats which had been fed 20 mg in 2 ml sesame oil of one of 9,10-dimethyl-1,2-benzanthracene (DMBA), 20-methylcholanthrene, benzanthracene, dibenzanthracene or benzpyrene, showed enhanced ability to convert 16-C¹⁴-estrone or estradiol (3.7×10^5 cpm in 10 μ g) to unidentified water-soluble products; phenanthrene had no effect. When admin. i.p., the carcinogens were ineffective; when admin. *in vitro*, low conc. of DMBA (1 μ g/ml) were inhibitory. Ethionine (50 mg in 2 ml of 0.9% saline) inj. i.p. 2 hr. before admin. of DMBA abolished the effect of the carcinogen. Pretreatment with carcinogen also resulted in the formation of at least 2 ether soluble compounds not present when C-14-estrogens were incubated with liver microsomes from untreated rats. Liver microsomes from rats with carcinogen-induced mammary tumors appeared to behave like those of normal hepatic tissue when incubated with C-14-estrogens.

- 63-453 INFLUENCE OF INITIAL TISSUE METABOLISM ON THE EXPERIMENTAL CARCINOGENIC PROCESS. (E.) Pozdnyakov, O. M. (Inst. Normal

Pathol. Physiol., USSR Acad. Med. Sci., Moscow). Nature (London) 198:699, 1963.

Soon after admin. of 9,10-dimethyl-1,2-benzanthracene (DMBA) to thoracic or femoral muscles of roosters, the activity of succinic dehydrogenase (SDH) was suppressed in both, but to a greater extent in white muscle; SDH activity was restored only in red muscle. Alterations of glucose-6-phosphate dehydrogenase (GDH) activity occurred in the same period, the level of activity changing in the opposite direction and to the same degree compared to SDH. Restoration of SDH activity coincided with lowering of GDH activity to initial levels. The reaction to, and resorption of DMBA were more pronounced in red muscle. SDH and GDH activities of fibers containing atypical cells corresponded to the activity of these enzymes in tumors. (See also CRA 1(2):#213, 1963.)

- 63-454 PARENCHYMAL CELL DAMAGE AND BILE DUCT ACTIVITY IN THE PRECANCEROUS LIVER. (E.) Sutton, P. M. (U. Coll. Hosp. Med. Sch., London). Brit. J. Cancer 16(4):619-625, 1962.

One group of Wistar rats were fed for 26 weeks with 0.06% dimethylaminoazobenzene (DAB); a 2nd in addition received weekly inhalations of CCl₄ for 21 weeks (weeks 3-14 and 18-26). In a group that received only the CCl₄, zones of liver necrosis occurred 24 hr. after admin. of the drug, but regeneration was complete within a week. In the two DAB groups, bile duct proliferation appeared and liver parenchymal cells were altered, forming hyperplastic nodules. Malignant tumors arose after about 6 mo. In the group subjected to DAB + CCl₄, bile duct activity was greatest and cholangiofibrosis developed earlier and more extensively than in the rats given only DAB. Both groups showed splenomegaly and the same incidence of liver cancer; therefore the increased cholangiofibrosis encountered when both agents were used was not considered a precursor of liver cancer. Some malignant tumors developed in the absence of cholangiofibrosis. Tumors varied histologically, and showed much necrosis, frequent mitoses and giant cells. The commonest finding was a pleomorphic pattern varying from hepatocarcinoma to adenohepatoma, a few being cholangiocarcinomas. Other tumors were wholly hepatocellular. The excess bile duct and portal tract proliferation following combined treatment is discussed along with the possible mechanisms: stimulation by autolytic tissue; specific activation by circulating factors; or damage to specific mechanisms controlling growth.

See also abstract nos.: 344,517,518

VIRAL CARCINOGENESIS

63-455 STUDIES ON THE TRANSMISSION AND TUMOR-INDUCING ACTIVITY OF THE MTA FROM TWO CANCEROUS STRAINS OF MICE. (E.) Bittner, J. J. (Dept. Path., U. Minn. Med. Sch., Minneapolis). Pp. 285-304 In The Morphological Precursors of Cancer. Severi, L. (Ed.). Perugia, Div. Cancer Res., 1962.

Results of inj. of extracts from lactating mammary glands of females from 2 inbred cancerous strains (A and Z(C3H)) into agent-free females of the 2 donor strains (Ax and Zb) and their F₁ hybrids were followed for several generations to obtain data on transmission and propagation of the agent by the experimental females and their offspring. Data were also analyzed for any change in the tumor-inducing properties of the admin. agents correlated with the genetic constitution of the animals, especially in back-cross hybrids derived by mating females of the F₁ generation with agent-free males of the agent-free stock. In ZBC test animals, the 2 extracts induced cancer in about 50% when admin. at 2 x 10⁻¹ dilutions. However, at 10⁻³ dilutions, strain A-MTA produced cancers in 92%, and strain Z-MTA in 38% of ZBC females. In the agent-free Ax strains, inj. of its own mammary tissue produced cancers in 24%; similar inj. of mammary tissue into Zb mice resulted in no cancers. In these experiments, strain Ax females transmitted the agent to 15%-47%, while strain Zb females transmitted the agent to 80% of their offspring. The earlier age of cancer incidence suggests that strain Z-MTA was more active than strain A-MTA in Zb females. In the AxZbF₁ hybrids, A-MTA induced cancers in 75%, strain Z-MTA in 27% of inj. females. Any difference in the tumor-inducing properties of the 2 agents in fostered F₁ hybrids and in their back-cross progeny appeared to be due to disappearance of the strain Z-MTA from a few inj. females, clearly indicating that some females of the fostered F₁ litters transferred the agent, while some litter mates did not. When the latter, and their progeny were omitted from totals born to infected mothers, F₁ mothers with A-MTA or with Z-MTA had incidences of 87%-89% and identical ages of tumor development. Potency of the agent did not appear to change with continued passage in susceptible mice.

63-456 TUMOR FORMATION IN TRANSPLANTED ORGANS OF POLYOMA-INOCULATED HAMSTER. (E.) Defendi, V. (Wistar Inst., Philadelphia) and J. F. Duplan. Arch. Path. 75(3):332-336, 1963.

Heart and kidneys from baby Lakeview hamsters inoculated at birth with polyoma virus were transplanted at intervals from 12 hr. to 14 days into the cheek pouches of 3-month-old Lakeview hamsters. Among the 71 recipients surviving for at least 1 mo., 9 had tumors which grew to 5-6 cm in diameter (3 heart and 6 kidney) after a latent

period of 34 days to 10 mo. Of these 9 tumors, 8 were from organs transplanted within 1-4 days after polyoma inoc. of the donors; some additional animals receiving transplants 8-14 days after infection showed nodules which persisted for about a mo. and then regressed. No tumors were observed in 5 mo. in 11 adult hamsters inoc. with polyoma virus instead of tissue. These results confirm that tumor induction by polyoma virus begins rapidly and that tumor growth is not markedly affected by the age of the host and can take place without the production of viral antibodies. It is concluded that these sarcomas developed from the transplanted tissue and not as the result of infection of the host by transplanted virus. In a later experiment (described in an addendum), involving transplantation of kidneys from infected females into adult males, analysis of the tumors for sex chromatin revealed a mixture of host and implanted tissue.

63-457 DETECTION OF A LEUKAEMOGENIC AGENT IN BALB/c MICE FOSTERNURSED BY RIII. PRELIMINARY REPORT. (E.) Squartini, F. (Div. Cancer Res., U. Perugia, Italy) and G. Rossi. Lavori Inst. Anat. U. Perugia 22(3):185-188, 1962.

Among male BALB/c mice foster-nursed by RIII females, upon autopsy, 14/29 had leukemia, developing at an average age of 290 days. All affected animals showed enlarged spleen and lymph nodes. Among 39 normally bred breeders, there were 3 leukemias and 1 tumor of the thymus. Two leukemias were observed in 19 forcibly bred females. In many cases there was diffuse lymphoid hyperplasia on autopsy of unaffected males or females. The low incidence of leukemias in females is thought to be due to the high incidence of mammary tumors (32/39 in breeding females, and 17/19 in forcibly bred females) leading to early death. Cell-free extracts from leukemic animals injected into 2-3-days-old BALB/c mice (4 females, 1 male) caused leukemia in all animals; the same extract failed to cause leukemia in 5 RIII mice 3-days-old. Since the incidence of spontaneous leukemia is low in the BALB/c and in the RIII strain, the data suggest that the Bittner virus carried in the RIII strain promotes mammary tumorigenesis and also leukemia in the BALB/c strain, or, alternately, that a latent leukomogenic virus carried by the RIII strain and transmitted via the milk has become active after transfer to BALB/c mice.

63-458 HORMONAL AND PHYSIOLOGICAL BACKGROUND IN THE PRODUCTION OF B PARTICLES BY THE MOUSE MAMMARY EPITHELIUM IN ORGAN CULTURES. (E.) Lasfargues, E. Y. (Dept. Microbiol., Columbia U., New York) and D. G. Feldman. Cancer Res. 23(2) (Pt.1):191-196, 1963.

Comparative studies of organ cultures of mammary

glands taken from mice of either the high-cancer RIII strain or the low-cancer C57BL strain during various stages of their first pregnancy showed that the production of B particles in RIII mammary glands is under hormonal control, and that the effect of the addition of hormones to the medium depends on the physiological status of the explants. The first of 2 peaks of higher production of B particles occurs in early pregnancy, is induced by an ovarian-hypophyseal combination; it corresponds to an active alveolar differentiation and growth of the epithelium. The second, during lactation, originates from the combined effects of 2 secretory inducing hormones (mammotropin and cortisol) and corresponds to a period of functional activity. In both cases B particle formation occurs in a phase of high protein synthesis and requires a physiologically intact cell. Absence of hormonal stimulation or an improper combination results in B particle inhibition. Duplicate cultures of agent-free C57 mammary tissues react morphologically to the various hormone combinations in the same fashion as the RIII's; however, no B particle is formed. This is considered further evidence that the viral particles in agent-positive RIII cultures might represent the milk factor.

63-459 STUDIES OF THE MECHANISM OF ACTION OF THE SHOPE RABBIT PAPILLOMA VIRUS.

I. CONCERNING THE NATURE OF THE INDUCTION OF ARGINASE IN THE INFECTED CELLS. (E.) Rogers, S. (U. Tenn. Mem. Res. Ctr., Knoxville) and M. Moore. *J. Exp. Med.* 117(3):521-542, 1963.

A comparison of the physicochemical characteristics of purified or partially purified arginases from various sources showed that Shope papilloma arginase is the same whether derived from wild or domestic rabbits, but differs strikingly from the other arginases tested. Thus, the papilloma arginase is unique in not requiring divalent ions for activation, indicating a different mechanism of action. Sucrose gradient and sedimentation studies indicate that papilloma arginase is a typical soluble protein, relatively soluble in water, with a high density and molecular weight but a helical or rod-like shape as opposed to the spherical shape of liver arginase. These results indicate that the virus-induced arginase in rabbit squamous epithelium is synthesized on the basis of information from virus DNA. Precipitin reactions between saline extracts of Shope papillomas induced in domestic rabbits by virus from a wild rabbit tumor and blood from domestic rabbits immunized against wild rabbit skin indicated the presence of a wild rabbit antigen presumably carried along by the virus DNA. Other experiments showing that the development of Shope papillomas is strongly inhibited by admin. of large doses of arginine in the presence of the arginase inhibitor canavanine indicate that viral DNA introduces into rabbit epithelium the information for the synthesis of an arginase for which the cells have no control mechanism. The arginase depletes cellular

arginine and, in turn, the synthesis of arginine-rich nuclear histones, thereby freeing the nucleus for greater synthetic activity and resulting in more rapid growth of the papilloma cells.

63-460 STUDIES ON THE STRUCTURE OF THE MAMMARY TUMOR-INDUCING VIRUS (BITTNER) AND OF LEUKEMIA VIRUS (GROSS). (E., Abstract) Dmochowski, L. (Univ. Texas M.D. Anderson Hosp., Houston), C. E. Grey, F. Padgett and J. A. Sykes. Pp. 6-7 In Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M.D. Anderson Hosp., Houston, February 20-22, 1963.

Application of the negative staining technic to high-speed centrifugal pellets prepared from suitably treated milk of C3H/Z, A/Jax, RIII/Dm high-mammary-cancer mice and milk of C3Hf, Af and C57 low-mammary-cancer mice revealed morphological similarities of the particles observed in both groups. Well defined surface projections were a characteristic feature, the over-all appearance being similar to that of the myxoviruses. The milk of low-cancer strain mice also contained virus particles which were more oleomorphic and variable in size and appeared to be surrounded by an additional membrane; bioassay of the milk of some of these preparations showed mammary tumor inducing activity. Examination of ultrathin sections of osmic acid-fixed, high-speed centrifugal pellets prepared from suitably treated milk of apparently healthy AKR high-leukemia-strain mice revealed characteristic virus particles resembling those seen in sections of leukemic organs. The virus particles showed well defined surface projections, resembling those found in cell free preparations from leukemic organs of rats inoculated with Gross leukemia virus. Similar spherical or doughnut-shaped virus particles have been found in sections of organs from embryos of AKR mice or 14-hour-old AKR mice, as well as in the spleen of 10-day-old and the bone marrow of 14-day-, 4-week-, 6-week- and 8-week-old AKR mice.

63-461 BIOLOGICAL AND STRUCTURAL PROPERTIES OF ROUS SARCOMA VIRUSES. (E., Abstract) Harris, R. J. C. (Div. Exp. Biol., Imperial Cancer Res. Fund, London). Pp. 25 In Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M.D. Anderson Hosp., Houston, February 20-22, 1963.

Studies of the capacity of strains of Rous sarcoma virus (RSV) to produce sarcomas in adult turkeys showed that RSV(B) and RSV(29) do not require the turkeys to have acquired the tolerance demanded by RSV(H), which apparently induces transplantation antigens in the infected turkey cell. These soluble, cell free antigens are related to the Forssmann and blood group A antigens and render 1-day-old poults susceptible to successful infection by RSV(H) in later life; they have not yet

been isolated, however, from ESV(H) chicken tumors or from the virus itself. The tolerant state so produced can be abrogated by homografts of lymphoid tissue from nontolerant turkeys. Finally, extracts of chicken tumors produced by the S-R strain of RSV have yielded hemorrhagic cysts and transplantable sarcomas in 1-day-old hybrid rats.

63-462 STUDIES ON BIOCHEMICAL, BIOPHYSICAL AND BIOLOGICAL PROPERTIES OF AVIAN TUMOR VIRUSES. (E., Abstract) Beard, J. W. (Dept. Surg., Duke Univ. Sch. Med., Durham, N.C.). Pp. 26-27 in Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M.D. Anderson Hosp., Houston, February 20-22, 1963.

Constitutional analysis showed that the BAI strain (myeloblastosis) virus was an RNA virus with no evidence of DNA, and had a high proportion of lipid and high P content. With respect to ultrastructure and amino acid composition, all the avian tumor viruses are essentially identical, but there are some differences in biological and immunological behavior, different strains being distinguishable on the basis of quantitative and qualitative aspects of the pathological manifestations, despite a broad overlapping of the spectra of neoplasms induced. The character of host response is affected by both the strain of virus and the nature of the host cell, as manifested by differences in the sites of virus synthesis and the manner of incorporation of cell constituents into the liberated virus particles. Sites of virus integration in the host cell are obscure, but some evidence suggests association of the determinative material of the BAI strain A with the precursors of the granules of the myeloid series in myeloblastosis. Studies of the nucleic acid metabolism of the myeloblasts indicate that viral RNA is synthesized from a soluble RNA fraction of the cell without direct involvement of the nucleus.

63-463 STUDIES ON CELLS INFECTED WITH AVIAN MYELOBLASTOSIS VIRUS. (E., Abstract) Berg, P. K. (Dept. Path., U. Colorado Med. Sch., Denver). Pp. 28 in Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M.D. Anderson Hosp., Houston, February 20-22, 1963.

Two types of tissue culture assay for avian myeloblastosis virus (AMV) were developed on the basis of the fact that chick fibroblasts infected with AMV *in vitro* were found to become resistant to superinfection with Rous sarcoma virus. Subsequent studies of the multiplication of AMV in chick fibroblast cultures showed that the first newly synthesized virus became detectable 24 hr.; during days 2 and 3 virus titer rose rapidly and then remained approximately constant. This was confirmed by studies with fluorescent antisera and to stain AMV antigens, most of the cell-

associated virus during this period was localized at the cell surface. The number of fluorescent foci which appeared in the cultures was found to be proportional to the virus concentration used for infection, approximately 10% of the infectious units forming foci of fluorescent cells.

63-464 INTERFERON IN RELATION TO TUMOR VIRUSES AND TUMOR CELLS. (E., Abstract) Allison, A. C. (Med. Res. Council, Natl. Inst. Med. Res., London). Pp. 34 in Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M.D. Anderson Hosp., Houston, February 20-22, 1963.

Interferon was found in 3 tumor virus-cell systems studied (polyoma, the Rous sarcoma, and avian lymphomatosis viruses). The presence of interferon may play a part in the persistence of virus and in the biochemical changes leading to transformation and/or selection which allow the emergence of tumor cell clones. The antiviral action of interferon was usually much weaker in tumor cells than in normal cells. Tumor cells often provided a favorable environment for persistent infections by interferon-sensitive viruses, both *in vitro* and *in vivo*. Because of the ease with which carrier situations can be established in tumor cells, special caution must be exercised about inferring that viruses found in such cells have played a part in the oncogenic process.

63-465 STUDIES ON THE ONCOGENICITY OF HUMAN ADENOVIRUS. (E., Abstract) Trentin, J. J. (Div. Exp. Biol., Baylor U. Coll. Med., Houston), Y. Yabe and H. G. Taylor. Pp. 40 in Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M.D. Anderson Hosp., Houston, February 20-22, 1963.

Systematic testing of human viruses for oncogenic properties showed that intrapulmonary injection of tissue culture fluid of human type 12 adenovirus into newborn hamsters produced a high incidence of malignant tumors at the site of inj. 1-3 mo. later. Extensive control studies showed a positive association between the tumor-inducing ability and the adenovirus content, and the tumor-inducing effect could only be neutralized by human antisera which also neutralized the adenovirus-type cytopathic effect. Tumors have also been produced by inj. of type 12 adenovirus into newborn hamsters via the intrapleural, i.p., s.c. and i.v. routes. The susceptibility of the hamsters to the induction of sarcomas at the site of inj. decreased rapidly with increased age at the time of inj., but for a given age the incidence of tumors induced was directly proportional to the dose of virus.

63-466 ONCOGENESIS BY AVIAN MYELOBLASTOSIS VIRUS. (E., Abstract) Baluda, M. A. (Dept. Biol., City Hope Med. Ctr., Duarte, Cal.).

Pp. 29 in Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M.D. Anderson Hosp., Houston, February 20-22, 1963.

Explants of hematopoietic tissues (spleen or yolk sac) from chick embryos or chickens, which did not multiply or differentiate by themselves, underwent a morphological conversion and multiplied after infection with avian myeloblastosis virus (AMV). The converted cells always resembled myeloblasts, regardless of the precursor cells in the explants, and some matured further into promyelocytes and myelocytes. These cells (which had a diploid set of normal chromosomes), produced AMV and multiplied exponentially for 1-3 mo. before beginning to degenerate. Virus production started within 24 hr. after infection, but conversion did not occur for several days, depending particularly on the temperature (maximal at 40°C). It was concluded that AMV behaves as an activator for some genes responsible for cellular division and differentiation into myeloid cells.

63-467 A CHILDREN'S CANCER DEPENDENT UPON ENVIRONMENT. (E., Abstract) Burkitt, D. P. (Dept. Surg., Makerere U. Coll. Med. Sch., Kampala, Uganda, Africa). Pp. 43-44 in Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M.D. Anderson Hosp., Houston, February 20-22, 1963.

The author describes the geographical distribution of a characteristic type of malignant lymphoma which affects children in the tropical areas of Africa and is manifested by multiple tumors in the jaws, kidneys, adrenals, liver and ovaries, which when untreated, is rapidly fatal. Since the maximal altitude of tumor distribution falls progressively as the distance from the equator increases, there seems to be a constant temperature dependence, with a minimal temperature of 60°F. In West Africa, where altitude varies little, there is a relation between tumor incidence and humidity; in both cases, the type of vegetation may play a role. This suggests that some vector is implicated in the transmission of the carcinogenic agent. If vector transmission is postulated, the possibility that the agent is a virus must be strongly suspected.

63-468 THE INTERACTION OF POLYOMA VIRUS WITH HAMSTER FIBROBLASTS. (E., Abstract) Stoker, M. G. P. (Inst. Virol., U. Glasgow, Scotland). Pp. 35 in Abstracts of Papers, 17th Ann. Sym. Fundl. Cancer Res.; Viruses, Nucleic Acids, and Cancer. M.D. Anderson Hosp., Houston, February 20-22, 1963.

Quantitative studies of the early events in neoplastic transformation by polyoma virus, using a cloned diploid strain of hamster fibroblasts as an assay system, showed that the virus has no obvious cytotoxic effect in these cells, and infectious virus was not produced, but 5%-10% of

the cells underwent neoplastic transformation. The remaining cells developed into normal clones despite virus penetration, and neither normal nor transformed clones showed residual virus. The transformation of single cells has been demonstrated, and selection of preexisting transformed cells has been excluded, so that transformation involves an inherited change which occurs before the first cell division. Transformation seems to be caused by the direct action of a single virus particle containing 7×10^6 molecular wt. units of DNA, which resembles particles with cytotoxic activity found in mouse cells. The sensitivity of individual cells to polyoma transformation, however, is affected by many factors.

63-469 A CONTRIBUTION TO THE STUDY OF POLYOMA VIRUS. (Fr.) Daniel, P. (Dept. Microbiol., U. Laval Fac. Med., Quebec). Laval Med. 34(3):336-343, 1963.

In a study of the special characteristics of polyoma virus production in monkey kidney cells, it was shown that the lack of a cytopathic effect (and the delayed cytopathic effect when such virus was transferred to mouse embryo tissue) was due neither to a low virus titer nor to the presence of an inhibitor of virus duplication, but apparently to attenuation of the virus itself. Differences between polyoma virus from monkey tissue and mouse embryo tissue were detected in the elution patterns from DEAE-cellulose columns. Detailed study of cell transformation produced by polyoma virus in mouse embryo tissue revealed that cell destruction began on the 7th day and continued to the 15th day, followed by a period of active growth of fusiform cells; in 3-4 weeks, the morphology changed and elongated cells appeared, most of which degenerated rapidly but some survived, so that the entire culture was overgrown by fibrocytic cells; in no case, however, was a permanent line produced. It was thus shown once again that *in vitro* susceptibility to polyoma virus cannot be predicted on the basis of *in vivo* response.

63-470 OBSERVATIONS ON TUMOR IMPLANTS INTO THE BODY AND ADNEXA OF THE CHICK EMBRYO. (Rus.) Sandor, S. (Lab. Exp. Embryol., Sci. Res. Ctr., Acad. R.P.R., Timisoara). Rev. Sci. Med. (Bucur.) 7(3-4):209-212, 1962.

Implants of benzpyrene-induced mouse sarcoma into the chorioallantoic membrane of 4-6-day-old Leghorn chick embryos failed to develop, and 6 days after implantation the remaining tumor cells were surrounded by a pronounced mesenchymal and epithelial reaction. In contrast, similar implant of mouse sarcoma into an artificial myelomeningocele in 3-day-old chick embryos yielded vigorous tumor growth. This difference is ascribed to differences in reactivity of the body and adnexa of the chick embryo. When Rous sarcoma and benzpyrene-induced mouse sarcoma were transplanted simultaneously to the chorioallantoic membrane of the chick embryo, the mouse sarcoma disappeared

completely while the Rous sarcoma became highly vascular, hemorrhagic and partially necrotic.

- 63-471 SKIN-APPENDAGE TUMORS INDUCED BY POLYOMA VIRUS IN MICE. (E.) Dawe, C. J. (NCI, Bethesda). Nat. Cancer Inst. Monogr. (10):459-487, 1963.

After polyoma virus (PV) infection of 100 mice (mostly C3H/Bi; others included C3H/f_g, DBA/2, AKR, RFM, (C3H/Lw x AKR)F₁ (AKR x C3H/Bi)F₁), the resultant skin-appendage tumors were almost invariably multiple. Attempts to transplant these benign tumors were unsuccessful in 17 recipients over 3-7 mo., except for one newborn mouse which probably received a large dose of PV with the tumor transplant. Comparison of these murine tumors with benign calcifying epithelioma in man showed some striking similarities of structure and development, though the human epithelium showed no viral inclusion bodies and less tumoral differentiation. The variable effects of these polyoma-induced pilosebaceous tumors and the probable mechanism of their developmental pattern are discussed, and a possible genetic interpretation is suggested for the diverse effects of PV on the ectodermal appendages. Comparison with the genetic syndrome of anhidrotic ectodermal dysplasia of man, and the remarkable overlap of involved organs with those of the PV-induced mouse tumors, are suggested as promising fields of investigation.

- 63-472 PHOSPHORUS METABOLISM IN VIRAL-INDUCED NEOPLASIA. I. STRAINS OF MICE SUSCEPTIBLE TO THE MAMMARY TUMOR VIRUS. (E.) McGregor, R. F. (U. N. Dakota Sch. Med., Grand Forks) and W. E. Cornatzer. Canad. J. Biochem. (4):985-991, 1963.

Uniform patterns of uptake of radioactive phosphate (25-35 μ C NaH₂P³²O₄, i.p. 2 hr. before sacrifice) into the phospholipids, nucleic acids and phosphoproteins of the liver, kidney and spleen were seen in both strain A (high-cancer) and BALB/c (low-cancer) female mice studied at the ages of 24, 31 and 64 days and at 10 mo. or more after the development of mammary tumors. Mammary glands from tumor-bearing strain A females, not yet containing tumors, exhibited increased phospholipid and nucleic acid synthesis compared to mammary glands from identical non-tumor-bearing strain A females, even though the tumor tissue itself showed lower activity. Thus there was significant differences in P metabolism between the 2 strains which may be due to a combination of virus and genetic factors. The liver, kidney and spleen showed the same activity in normal and tumor-bearing mice. Since the virus itself had no effect on phosphorus metabolism in the mammary glands, it seems that mammary tumor virus stimulates phospholipid synthesis immediately prior to tumor development, in a manner analogous to acute infectious viruses.

- 63-473 STUDIES ON THE VIRUS OF RABBIT PAPILLOMA. I. METHODS OF ASSAY. (E.) White, D. O. (Sch. Bact., U. Melbourne), R. J. Huebner, W. P. Rowe and R. Traub. Aust. J. Exp. Biol. Med. Sci. 41(Pt. 1):41-50, 1963.

Assay methods for rabbit papilloma virus (RPV) are described which employ mechanical skin scarification or abrasion, shaving, plucking, and keratin removal with adhesive cellulose tape; the method of choice was a combination of the last two; the most complete tumor counts were made between 30 and 35 days. Attempts to cultivate RPV in other systems were not successful (tumor production in other mammals, inoculation in embryonated eggs, tissue cultures and various growth media). No interference phenomena developed on challenge with other viruses. Nucleic acid extracts in human skin fibroblast cultures did not lead to virus multiplication; hemagglutination and hemadsorption could not be demonstrated. Rabbits inoculated with 100 ID₅₀ of RPV on each of 20 sites showed, by successive excisions, some residual infectious virus on the inoculation sites for a few days, then none for 3 weeks until tumors appeared; then virus and tumors increased together. Thus the virus appears to be solely responsible for the initiation and early maintenance of the tumor.

- 63-474 A STUDY OF THE ISOLATION OF LEUKEMIA VIRUS OF AKR MOUSE BY FLUOROCARBON. (E.) Okada, K. (Dept. Int. Med., Okayama U. Med Sch., Japan) and I. Miyoshi. Acta Med. Okayama 16(5):232-237, 1962.

A new improved method for the isolation of AKR mouse leukemia virus is described, using trichlorotrifluoroethane for separation of the virus from soluble proteins and lipids. The aqueous layer, inoc. s.c. or i.p. (0.03-0.1 ml) into 23 newborn AKR mice induced lymphatic leukemia in 8/23 at 3-5 mo. of age. Spontaneous leukemia in 58 AKR controls developed only after the age of 6 mo., with a peak incidence at 9-10 mo. Subsequent passage of virus, partially purified by the same method, continued to cause leukemia when inoc. into newborn AKR mice (1/5, at age 2 mo.). A virus preparation obtained by the fluorocarbon extraction method had an O.D.₂₆₀ of 1.65 and contained 51 μ g/ml of RNA and 0.05 μ g/ml of DNA, suggesting that the virus is of the RNA type.

- 63-475 ANALYSIS OF ACQUIRED TOLERANCE TO THE ROUS SARCOMA VIRUS IN DUCKS. IV. QUANTITATIVE FINDINGS ON THE COURSE OF TOLERANCE, THE FORMATION AND EFFECT OF VIRUS NEUTRALIZING ANTIBODIES AND TESTS OF TOLERANCE BY VIRUS FILTRATES AND PREPARATIONS OF KNOWN ACTIVITY. (E.) Svoboda, J. (Inst. Exp. Biol., Acad. Sci. CSSR, Prague). Folia Biol. (Praha) 8(3):133-139, 1962.

Tolerance to Rous sarcoma virus (RSV) was obtained in Peking ducks by the use of cell free RS filtrates and the microsomal fraction isolated from a Rous tumor of known activity. Increased susceptibility of birds tolerant to RV, in comparison with controls, was observed on the 8th day of life, but was most pronounced between days 16 and 19, when over 50% of the tolerant birds inoc. with tumor filtrates died from tumors, while the controls survived. The smallest amount of fowl blood required for induction of tolerance (mortality = 10%) was 0.3 ml, admin. on the first day of life. A higher degree of tolerance (mortality = 30%) was obtained if this was divided into 3 doses, given on days 1, 3, and 5. Similar results were obtained with 0.9 ml of chicken blood. The neutralizing capacity of sera from tolerant birds with progressively growing tumors did not differ significantly from that of the negative controls, both showed ID₅₀ within the range of 10^{-2.16} to 10^{-3.23} after incubation of sera with RSV. The repeated passive transfer of duck antisera against RS to ducklings with a neutralizing index of 5 did not abolish or lower the tolerance as compared with the controls. Results are consistent with the hypothesis that on infection of heterologous cells the RV induces the formation of fowl antigens in it, so that the tumor cells can grow only in immunologically immature birds or in birds tolerant to these antigens.

- 63-476 FURTHER FINDINGS ON THE INDUCTION OF TUMOURS BY ROUS SARCOMA IN RATS AND ON THE ROUS VIRUS-PRODUCING CAPACITY OF ONE OF THE INDUCED TUMOURS (XC) IN CHICKS. (E.) Svoboda, J. (Inst. Exp. Biol., Acad. Sci. CSSR, Prague). *Folia Biol. (Praha)* 8(4):215-220, 1962.

A group of rats inoculated after birth with Rous sarcoma showed, after a 2 year follow-up, two more sarcomas, XCBK which appeared at 22 mo. on the back of a male which also had a hemorrhagic cyst, and tumor R2 formed at 25 mo. in a female also s.c. in the back, and which also had a benign mammary adenoma. All three primary tumors were completely inactive when transferred to chicks. The 6th and 8th passages of the two sarcomas were also inactive in chicks. With the addition of these two sarcomas, the total incidence of sarcomas in the rat group increased to 8%. Sarcoma XC, previously described from this group of rats, was found to grow equally well in preimmunized and non-preimmunized animals. In both, the tumors were detectable by the 9th day after transplantation, and 4/5 of the tumors induced sarcomas when admin. to chicks. Cell-free extracts of one of these fowl tumors had an ID₅₀ of $5 \times 10^{-3.77}$ and duck antisera against Rous fowl virus showed a neutralization index of 2.11. However, the XC tumor from rats could induce tumors in chicks only when living cells were inj.; irradiation of tumor suspensions with 50,000 or 10,000 r decreased its infectivity.

- 63-477 STUDIES IN THE EPIDEMIOLOGY OF MYXOMATOSIS IN CALIFORNIA. II. THE EXPERIMENTAL TRANSMISSION OF MYXOMATOSIS IN BRUSH RABBITS (*SYLVILAGUS BACHMANI*) BY SEVERAL SPECIES OF MOSQUITOES. (E.) Grodhaus, G. (Bureau Vector Control, Cal. State Dept. Pub. Health, Berkeley), D. C. Regnery and I. D. Marshall. *Am. J. Hyg.* 77(2):205-212, 1963.

Myxomatosis from a California strain of myxoma virus was transmitted serially among brush rabbits (*Sylvilagus bachmani*) and transferred to domestic rabbits (*Oryctolagus cuniculus*) by female *Anopheles freeborni* and 4/5 other species of mosquitoes, by a technic of interrupted feeding. Tumors were induced at all feeding sites except the ears, and the tumors remained infective for mosquitoes usually for 30-40, sometimes up to 86 days after transmission. In *Sylvilagus*, tumors regressed after about 3 weeks; all 20 *Oryctolagus* died from 6-20 days after mosquito-borne virus infection from the brush rabbits.

- 63-478 STUDIES IN THE EPIDEMIOLOGY OF MYXOMATOSIS IN CALIFORNIA. III. THE RESPONSE OF BRUSH RABBITS (*SYLVILAGUS BACHMANI*) TO INFECTION WITH EXOTIC AND ENZOOTIC STRAINS OF MYXOMA VIRUS, AND THE RELATIVE INFECTIVITY OF THE TUMORS FOR MOSQUITOES. (E.) Marshall, I. D. (Dept. Microbiol., Australian Natl. U., Canberra) and D. C. Regnery. *Am. J. Hyg.* 77(2):213-219, 1963.

After inoc. of brush rabbits (*Sylvilagus bachmani*) with endemic California (C) and South American (SA) strains of myxoma virus, benign tumors were induced; both were rated as approximately 99% lethal to the domestic rabbit (*Oryctolagus cuniculus*). The attenuated Australian (AA) strain produced only barely detectable thickenings at some inoc. sites in the brush rabbits but is about 60% lethal in the domestic rabbit. Transmission of the myxoma virus by mosquitoes was successful in 80% with the C strain, but failed completely with the SA strain. The difference appears to lie in the virus content of the donor tumors: titrations showed 10⁸ rabbit-infectious doses (ID) of C strain virus per g of tumor tissue, but only approximately 10⁴ ID/g in SA strain tumors. The brush rabbit requires 100-1000 times as many AA virus particles as does the domestic rabbit, this being a greater amount than the mosquito can carry. These two barriers determine the very high degree of specificity in the mutual adaptation of host and parasite in the brush rabbit and the endemic California myxoma virus strain. (See also CRA 1(3):#538, 1963.)

- 63-479 THE EFFECT OF SAPONIN AND DIGITONIN ON ROUS SARCOMA VIRUS AND CELL MEMBRANES; AN APPROACH TO THE CYTOCHEMISTRY OF CELLULAR COMPONENTS BY THE USE OF NEGATIVE STAINING. (E.) Dourmashkin, R. R. (Div. Exp. Biol. Virol., Imp. Cancer Res. Fund., London, N. W. 7), R. M. Dougherty and R. J. C. Harris. *J. Roy. Micr. Soc.* 81(Pt. 3 & 4):215-218, 1963.

Cell membranes of chick liver cells of RSV and of erythrocyte ghosts treated with saponin and examined in the electron microscope by the negative staining method all presented a similar array of pits about 8.0 μ m in diameter and spaced 14-16 μ m apart, surrounded by a ring compressed on six sides by neighboring rings. The optimal concentration of saponin was 0.05% (10 ml/1 ml of packed erythrocytes). Further treatment of saponin-treated ghosts with trypsin or pepsin led to enhancement of image contrast. Treatment with digitonin inhibited the action of saponin on pit formation quantitatively, suggesting that the digitonin had combined with cholesterol present in the membranes in such a way as to prevent the action of saponin. The appearance of identical structures in cell and viral membranes suggests a common basic architecture.

63-480 MORPHOLOGICAL AND VIROLOGICAL INVESTIGATION OF HUMAN TISSUE CULTURES TRANSFORMED WITH SV40. (E.) Pontén, (Wistar Inst. Anat. Biol., Philadelphia), F. Jensen and H. Koprowski. *J. Cell. Comp. Physiol.* 1(2):145-163, 1963.

Infection by SV40 (simian virus 40) of human organ cultures and monolayers of human diploid fibroblasts (HDCS) at different subculture levels was followed by transformation of all infected cultures. Transformation of monolayers of pure fibroblasts indicated that such cells can change morphologically into epithelial-like cells. Non-infected control cultures maintained under the same conditions showed a regular fibroblastic pattern. Infected cultures went through 3 phases: cytopathic (2-4 weeks), early transformation (several weeks) and complete transformation. Foci of epithelial-like cells which appeared during early transformation supplanted the fibroblasts at the complete transformation phase. When mass cultures were cloned, none of the fibroblasts contained virus, whereas virus was released in the epithelial clones studied. Only 1 but 2 transformed cultures remained infectious. The SV antigen, present in a small percentage of transformed cells, was always localized in the nucleus by immunofluorescence.

63-481 VIRUS-LIKE PARTICLES IN THE LYMPHOCYTES OF A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA. (E.) Zucker-Franklin, D. (Dept. Anat., New York U. Sch. Med.). *Blood* 21(4):509-512, 1963.

Lymphocytes from the peripheral blood of a patient with chronic lymphocytic leukemia were isolated and subjected to electron microscopy. Aggregates of virus-like particles measuring 8-12 μ m in diameter were observed as organized structures in the cytoplasm of the cells. The longitudinal sections of the particle aggregates resemble those described in ECHO 9 virus infected tissue culture cells, but the patient had no clinical signs of the disease and viral agglutination studies

were negative. The particles also resemble the "sticks" described by Bernard et al. in a patient with long standing chronic lymphatic leukemia. The present patient had leukemia for 20 years, and has received intermittent splenic irradiation and chlorambucil, but no treatment during the 2 years preceding the study. The particles were limited to lymphocytes and were found on 3 occasions. The blood samples were taken at monthly intervals at a time when WBC decreased spontaneously from 24,000 to 8,000.

63-482 EFFECT OF VITAMIN B₁₂ ANILIDE ON THE PRODUCTION OF HEMORRHAGIC LESIONS IN THE CHICK EMBRYO FROM ROUS SARCOMA VIRUS INFECTION. (E.) Iccayan, E. E. *J. Philipp. Med. Assn.* 39(2):142-145, 1963.

Admin. of vitamin B₁₂ anilide via the yolk sac prior to i.v. inoc. of 11-day chick embryos with Rous sarcoma cell free extracts caused a significant diminution in the number of hemorrhagic lesions/embryo. Mean values for hemorrhagic lesions/embryo and for the hemorrhagic liver lesions/embryo, resp. were: controls, 17.2 and 9.62; 250 μ g B₁₂ anilide, 10.3 and 3.54; 0.5 μ g B₁₂, 18.3 and 8.09; and 0.5 μ g B₁₂ + 250 μ g B₁₂ anilide 16.0 and 4.7. The mechanism of this process remains to be elucidated.

63-483 PHYSICAL CHARACTERISTICS OF POLYOMA VIRUS. III. CORRELATION WITH BIOLOGICAL ACTIVITIES. (E.) Abel, P. (Inst. Genet., U. Cologne, W. Germany) and L. V. Crawford. *Virology* 19(4):470-474, 1963.

Equilibrium density gradient studies of polyoma virus P54 in RbCl showed 2 peaks of hemagglutinating activity: that at 1.32-1.33 was found to contain "full" particles on electron microscopic examination, and to show good agreement between hemagglutinating, plaque forming and, to a lesser extent transforming activity (the peak for the latter was 1.325). The second hemagglutinating activity peak at 1.29-1.30 contained essentially "empty" particles; they had no plaque forming activity and negligible amounts of transforming activity. Further attempts to increase the separation between hemagglutinating and transforming activity in the 1.32-1.33 fraction were unsuccessful; good agreement was obtained between these two fractions on subsequent re-equilibration.

63-484 ELECTRON MICROSCOPY OF "YABA VIRUS". (E., Abstract) Owens, G. (Roswell Park Mem. Inst., Buffalo), R. Metzgar and J. T. Grace, Jr. *Clin. Res.* 11(2):212, 1963.

After i.v. inj. of Yaba virus, tumors of histiocytic origin were observed in the subcutaneous tissue, heart, lungs and skeletal muscles of susceptible animals. Electron microscopy of both human and monkey subcutaneous lesions showed

brick-shaped intracytoplasmic particles 250-330 m μ in size, similar in morphology to viruses of the pox type. Fluorocarbon treatment of virus pellets produced marked structural alterations of the virus particles and reduced their infectivity and antigenicity. (See also CRA 1(2):#268, 1963.)

- 63-485 UNUSUAL NUCLEAR LESIONS AND CYTOPLASMIC INCLUSIONS IN TWO CASES OF HUMAN LYMPHORECTICULOSARCOMA. (Fr.) Vasquez, C. (Inst. Hemat. Invest., Nat. Acad. Med., Buenos Aires), A. Pavlovsky and W. Bernhard. C. R. Acad. Sci. (Paris) 256(10):2261-2264, 1963.

Electron micrographs of lymphoblasts from the lymph nodes of 2 pts. with lymphoreticulosarcoma revealed two types of lesions, one nuclear and the other cytoplasmic; they were never observed in the same cells, and the nuclear lesions were less frequent. The nuclear changes consisted of sharply defined chromatin and of one or 2 aggregates of homogeneous electron-dense particles 15-25 m μ in diameter. The aggregates were at times adjacent to the nucleolus, at times away from it. The cytoplasmic lesions consisted of vacuolar inclusions 1-2 μ in diameter surrounded by a membrane, which in some places appeared to be doubled. The individual particles were homogeneous, but contained no nucleoid. Isolated projections were observed in the walls of the vacuoles, and may be involved in particle formation. The findings are discussed in terms of the possible reflection of degenerative processes or the possibility that some of the inclusion particles may represent virus particles.

- 63-486 PRESENCE OF VIRUS-LIKE PARTICLES IN ORGAN TISSUE CULTURES OF HUMAN CANCERS. (Fr.) Zagury, D. (Lab. Electron Microscopy Appl. Biol. CNRS, Paris). C. R. Acad. Sci. (Paris) 256(13):2951-2954, 1963.

Virus-like particles of 80, 90, 95 and 75 m μ were found in the cytoplasm and the extracellular spaces of organ tissue cultures of tumor Z 159 (hepatic metastasis of a gastric cancer), Z 266 (cancer of the stomach), Z 237 (cancer of the bladder) and two samples of different passages of Z 200 (a hepatic metastasis of a gastric cancer) carried for 8 and 35 passages, resp. Cellular alterations were detected in all cultures.

- 63-487 ISOLATION, PROPERTIES AND LEUKEMOGENIC ACTIVITY OF NUCLEIC ACIDS FROM VIRUS-INDUCED MYELOID LEUKEMIA. (Ger.) Bielka, H. (Inst. Exp. Cancer Res., Germ. Acad. Sci. Berlin, Berlin-Buch), A. Graffi and Chang Yü Yen. Acta Biol. Med. German. 10(1-2):63-78, 1963.

When various nucleic acid preparations from the enlarged lymph nodes or thymus of leukemic mice

were inj. (usually 0.2-0.3 ml s.c., sometimes 0.1 ml i.p. or 0.02 ml intracerebrally) into newborn mice, leukemia developed within the 10 mo. av. latent period in 14/82 given RNA from mice with primary virus-induced leukemia, 6/23 given RNA from transplantable myeloid leukemia (SOV16 tumor growing i.m. or i.p.), 0/31 given RNA after treatment with RNase, 10/275 given protein-free DNA preparations, and 11/127 given DNA preparations containing protein (and possibly RNA). Spontaneous incidence of leukemia was 1/668; incidence in newborn mice given filtrates of mouse, rat or chicken embryonic tissue was 2/113; incidences in mice given whole filtrates from leukemic leukocytes (0.1 ml s.c.) were 23/53 and 45/61 (2 experiments). This indicates that intact RNA is necessary for the transmission of virus-induced leukemia in mice. The base ratios and some of the physical properties of the nucleic acid preparations are also reported.

- 63-488 OBSERVATIONS ON THE HAEMORRHAGIC DISEASE INDUCED BY FOWL TUMOUR VIRUSES. (E.) Carr, J. G. (Agr. Res. Council Poultry Res. Ctr., Edinburgh, Scotland). Brit. J. Cancer 16(4): 626-633, 1962.

Brown Leghorn fowls inoculated with a variety of fowl viruses and with non-virus associated tumors were analyzed in order to determine the etiology and mechanism of hemorrhagic disease. In a study of age susceptibility, those viruses which caused hemorrhagic disease in chicks over 4 weeks old included CHF 1, Duran-Reynals "D"; those less than 4 weeks old, Rous sarcoma 1, Fujinami, PRC 3 and ES 4; and those only affecting embryos, MH 2 and PRC 4. No hemorrhagic disease could be detected when chicks of any age were inoculated with non-virus tumors such as GRCH/15 or CRCH/16 sarcoma, or with 4 new transplantable sarcomas including PRC 7. After i.m. inj. of virus into 3-day-old chicks, minimum time requirement for appearance of the disease was about 18 days. Failure to find hemorrhagic disease in birds dying after 25 days could have been due to resorption of the lesions. The site of the hemorrhagic lesions was primarily in tumor, liver, pancreas, and duodenum or, more generally, in areas of extramedullary hematopoiesis. In older birds, hemorrhagic disease was found in the partially absorbed yolk sac and in embryomas produced by inoculation of homogenates from young fowl. These localizations strongly suggest that hemorrhagic disease is not related to the necrotic action of the virus on the endothelium of the vascular system but is due to viral destruction of endothelium in areas of extramedullary hematopoiesis.

- 63-489 MULTIPLICITY OF CELL RESPONSE TO THE B. STRAIN A (MYELOBLASTOSIS) AVIAN TUMOR VIRUS. III. HISTOLOGIC ALTERATION AND ADENOSINETRIPHOSPHATASE ACTIVITY OF THE THYMUS OF CHICKENS WITH MYELOBLASTOSIS. (E.) Arvy, L. (Dept. Surg. Path., Duke U. Med. Ctr., Durham, N.C.), J. R. Sommer, G. De Thé, U. Heine,

Ishiguro, D. Beard and J. W. Beard. J. Nat. Cancer Inst. 30(3):401-413, 1963.

Chicks infected with BAI strain A (myeloblastosis) virus, the normal population of lymphocytic cells of the thymus cortex was replaced by blast-like elements. These cells appeared to originate in small foci in the cortex and pervaded the cortical tissue in an orderly, uniform manner. There was no enlargement of the thymus or other evidence of neoplastic change. The medulla was unaltered. In contrast to the normal, there was a strong, positive adenosinetriphosphatase reaction in the cortex, related to enzyme activity at the cytoplasmic membrane of the blast-like cells. Alterations in cell population and enzymatic reaction analogous to those of the thymus were not shown in the tissue of the bursa of Fabricius, spleen, or other organs examined. Similar studies of birds with erythroblastosis did not reveal the phenomena observed in myeloblastosis. The data suggest that the cells were derived from sources intrinsic to the thymus. The virus may affect lymphic cells more primitive than the lymphocytes or reticular cells and yield a population of blast-like cells with different properties from those of normal thymus cells.

490 MULTIPLICITY OF CELL RESPONSE TO THE BAI STRAIN A (MYELOBLASTOSIS) AVIAN TUMOR VIRUS. IV. ULTRASTRUCTURAL CHARACTERS OF THE THYMUS IN MYELOBLASTOSIS AND OF THE ADENOSINETRIPHOSPHATASE ACTIVITY OF THYMIC CELLS AND ASSOCIATED VIRUS. (E.) De Thé, G. (Dept. Surg. Path., Duke U. Med. Ctr., Durham, N.C.), Heine, J. R. Sommer, L. Arvy, D. Beard and J. W. Beard. J. Nat. Cancer Inst. 30(3):415-455, 1963.

Further ultrastructural studies of the blast-like cells found in the thymus cortex of chickens with myeloblastosis showed large cytoplasmic nuclear ratios, and an extensive Golgi region. (See preceding abstract.) Associated with the Golgi were spherical structures with a central electron-dense region, 65-85 m μ in diameter, surrounded by a thin, dense ring, and enclosed in a less dense structure 10-12 m μ in thickness. The spheres resembled the type A-2 particles found in some plasma cell mouse tumors and in normal liver cells observed by others. Occasionally budding of the cell membrane of the blast-like cells suggested virus elaboration, but no direct relation was found between the spherical structures and the virus budding. There was no virus formation in reticular cells. Adenosinetriphosphatase activity was present at the cytoplasmic membranes of the large cells replacing lymphoid cells of the normal thymus, and also at the surface of individual virus particles. The findings suggest that the source of enzyme is cell membrane incorporated in the virus in the process of budding. In erythroblastosis induced by strain R, the thymus failed to show the specific changes found in myeloblastosis. Lymphomatosis cells found in the

liver of infected birds differed from the cells of the thymus affected by the same agent. The cells of lymphomatosis were nearly spherical, sometimes deeply indented, with dispersed chromatin and a prominent nucleolus. Centrioles and Golgi complex were rarely identified. There was no budding of virus in the cell membrane and the few invaginations in the cytoplasmic membrane were unlike those in the thymus cells.

63-491 FLOCKS OF CHICKENS FREE FROM ANTIBODY TO ROUS VIRUS. (E.) Bang, F. B. (Johns Hopkins U. Sch. Hyg. Publ. Health, Baltimore) and M. Foard. J. Nat. Cancer Inst. 30(3):457-466, 1963.

A flock of chickens entirely free from antibodies to Rous virus (RV) was maintained for 2 yr. through 3 generations. The initiating eggs were from an open flock that had been isolated for 6 mo. These eggs were hatched and the chicks were raised in isolation. Such chicks were readily infected with RV and developed antibodies to it. After inoculation with the Harris (British) strain of RV, they did not develop antibodies to the Bryan (American) strain of RV. When these birds were placed in close contact with chickens with experimentally induced tumors, 2/9 developed antibodies but none developed tumors. None of the progeny developed antibodies when kept in rooms with open flock chickens or when raised from the age of 3 days with open flock age mates. The same proportion of embryos was resistant to RV in the antibody-free flock as in the open commercial flock. These embryos were completely resistant to virus after infectious doses varying from 10 to 200. Analysis of the embryo resistance derived from individual antibody-free and open-flock hens is compatible with the interpretation of resistance as a single recessive character and excludes a single dominant but no multifactorial characters.

63-492 ATTEMPTS TO OBTAIN VIRUS-FREE ROUS TUMORS IN TISSUE CULTURE. (E.) Rabin, H. (Johns Hopkins U. Sch. Hyg. Publ. Health, Baltimore), C. F. A. Heijen, M. Foard and F. B. Bang. J. Nat. Cancer Inst. 30(3):467-476, 1963.

Attempts to free Rous tumors from infectious virus were made by serial alternate passages of the tumor in tissue culture in the presence of antiviral antibody. Also lowering the temperature of *in vitro* incubation to 32°C was found to inhibit virus multiplication. The virus-inhibited cultures were then inoculated into chickens in the presence of antiviral antibodies. In 3/4 occasions subsequent tumors grew in tissue culture without producing detectable amounts of virus. However, continued serial alternate passage yielded virus up to the 25th passage, at which time the study was discontinued. On incubation at 30° or 32°C, virus yields from primary explants of tumors on collagen were markedly decreased, or was undetectable. Virus growth in temperature-inhibited cultures was stimulated by return to 38°C.

Cultures of 2 tumors were impaired in their ability to produce tumors after growth at 32°C, but subsequent tumors obtained by inoculation of chickens contained large amounts of virus.

- 63-493 ORIGIN AND DISTRIBUTION OF VIRUS-LIKE PARTICLES ASSOCIATED WITH MAMMARY TUMORS IN DBA STRAIN MICE. I. VIRUS-LIKE PARTICLES IN MAMMARY GLAND TISSUE. (E.) Feldman, D. G. (Rockefeller Inst. Med. Res., New York). *J. Nat. Cancer Inst.* 30(3):477-501, 1963.

Neither A nor B particles were found in the mammary glands of strain DBA virgin mice less than 6 mo. of age, however, both were found after age 6 mo. Both A and B particles were also found in 3-month-old females during their first pregnancy and lactation, and during the resting stage after the first pregnancy. Both particles were also present in the tissue of pregnant or lactating agent-carrying RIII and (C3H x A)F₁ x C3H mice, but were not in the tissues of agent-free C57BL and (C3H x A)F₁ x C3H females. The present evidence is consistent with a participation of A particles in the formation of B particles which may, in turn, represent the mammary tumor agent.

- 63-494 ORIGIN AND DISTRIBUTION OF VIRUS-LIKE PARTICLES ASSOCIATED WITH MAMMARY TUMORS IN DBA STRAIN MICE. II. VIRUS-LIKE PARTICLES IN THE BLOOD AND ORGANS. (E.) Feldman, D. G. (Rockefeller Inst. Med. Res., New York). *J. Nat. Cancer Inst.* 30(3):503-515, 1963.

Examination of tissue from lung, liver, kidney, spleen, testis, seminal vesicle and epididymis of strain DBA mice failed to reveal A or B particles. One B particle was seen in a capillary of a spontaneous tumor. However, a fluorocarbon extract of blood from a tumor-bearing mouse showed many B particles. Particles resembling the A bodies seen in mammary tumors were found in the endoplasmic reticulum of the epididymis of both the high-cancer DBA strain and of agent-free C57BL males. The absence of B particles from a variety of tissues possessing bioactivity and their presence in blood suggests that if B particles are the mammary tumor agent, infectivity of organs may be due to the presence of low concentrations of the particles in the blood supply to these organs.

- 63-495 ORIGIN AND DISTRIBUTION OF VIRUS-LIKE PARTICLES ASSOCIATED WITH MAMMARY TUMORS IN DBA STRAIN MICE. III. VIRUS-LIKE PARTICLES IN TRANSPLANTED TUMORS. (E.) Feldman, D. G. (Rockefeller Inst. Med. Res., New York). *J. Nat. Cancer Inst.* 30(3):517-531, 1963.

Two series of transplanted mouse tumors in males, one from passage 1-20, and the other from passage

32-45, were examined with the electron microscope. The original spontaneous tumor from a DBA female contained many A and B particles. Mature B particles with nucleoid were seen only up to the passage 3, although occasionally there were budding and detached B particles without nucleoids in subsequent passages. The A particles persisted through all passages. During the transplantation the tumors dedifferentiated from an acinar to a solid alveolar type. Since the B particles appear to mature only in acinar, or intracellular spaces, or in vacuoles, it is possible that with dedifferentiation of the tumors, B particles lost the space required to mature.

- 63-496 STRUCTURE OF THE GROSS LEUKEMIA VIRUS. (E.) Parsons, D. F. (Ontario Cancer Inst., Toronto, Canada). *J. Nat. Cancer Inst.* 30(3):569-583, 1963.

Gross virus was investigated by the technic of negative staining of partially purified preparations; it was also examined *in situ*, in and around leukemic cells by a modification which permits the negative staining of cells thinly spread on a water interface. By the use of both methods the nucleoid was clearly outlined in some type C particles; its surface was smooth without projecting capsomeres. No filamentous components, similar to those seen in myxoviruses, were found in association with the nucleoid after treatment with formaldehyde, ether, pepsin or trypsin. Negative staining also indicated that the Gross virus resembles Rous sarcoma virus in possessing an envelope covered with a fringe of fine projections. This fringe differed markedly from that covering the envelope of the mouse mammary tumor virus. It is suggested that the classification of murine tumor viruses into types A, B, and C should be extended to take these differences of envelope structure into account.

- 63-497 COMPARATIVE VIRULENCE OF THE MAMMARY TUMOR AGENT FROM DIFFERENT SOURCES; QUALITATIVE AND QUANTITATIVE DIFFERENCES. (E.) Hummel, K. P. (Roscoe B. Jackson Mem. Lab., Bar Harbor, Maine) and C. C. Little. *J. Nat. Cancer Inst.* 30(3):593-604, 1963.

The virulence of the mammary tumor agent (MTA) in males and in parous and virgin females of C3H, RIII, A, and DBA/1 mice was compared by inoc. of groups of young female mice of low tumor strain BALB/c with blood derived from the 12 groups of donors. The qualitative nature of the MTA difference was determined by observation of tumor rates, incidence and mean tumor age, in female offspring of the inoc. mice. In both inoc. BALB/c mice and their offspring, the groups with MTA derived from strain C3H mice had more tumors at younger ages than groups with MTA derived from the other high-tumor strains. These observations are evidence that the MTA carried in the blood of strain C3H mice differs in

quality from that in mice of strains R111, A, and DBA/1; it is a more virulent form, inducing early development and a high incidence of mammary gland tumors in the BALB/c mice. The groups of BALB/c mice inoc. with blood from multiparous females had higher tumor rates than those with blood from virgin females and males, but tumor rates in the offspring of the 3 groups were not different. This observation is interpreted as evidence that, although there is more MTA in the blood of multiparous females, it has not been changed in a detectable qualitative way by the hormonal output of the donor.

-498 MODIFICATION OF ONCOGENIC EFFECTS OF S-POLYOMA VIRUS BY "ATTENUATED" POLYOMA VIRUS. (E.) Law, L. W. (NCI, Bethesda) and A. S. Rabson. J. Nat. Cancer Inst. 30(3):635-641, 1963.

An attenuated polyoma virus variant (M polyoma) was used to modify the response of C3Hf/Bi mice to the highly oncogenic variant (S polyoma) of identical origin but maintained on P388 D1 cells under different culture conditions. When C3Hf/Bi mice less than 24 hr. old received M virus, followed by S virus at 10 days of age, only 37 (8%) developed polyoma-type tumors. Few primary sites of tumor induction were observed. In contrast, recipients of control tissue culture medium on the day of birth, followed by S-polyoma virus on the 10th day, developed polyoma-type tumors in 19/40 (47.5%), at as early as 3 mo. There were many primary tumor sites were seen, and lesions of the renal-cortical tubules were both common and severe. Neutralizing and hemagglutination-inhibiting antibody titers were low in C3Hf/Bi mice at the time of induction of S virus, but reached high levels by day 20-30. Two possible mechanisms are discussed, suppression of oncogenicity of S virus as a result of viral antibody produced by infection with the M virus or, alternately, an effect due to viral interference or to "interferon" production.

-499 MA/My STRAIN OF THE MARSH ALBINO MOUSE. (E.) Murray, W. S. (Roscoe B. Jackson Mem. Lab., Bar Harbor, Maine). J. Nat. Cancer Inst. 30(3):605-610, 1963.

On 424 treated and 920 untreated females of the MA/My derivative of the high mammary tumor incidence Marsh albino mouse strain indicate that the substrain carries no virus-like mammary tumor or milk agent, although susceptible to it when foster nursed by C3H/He females. The MA/My mammary tumor agent-free strain arose without experimental manipulations, and has remained agent-free for 30 generations.

-500 THE TRANSPLANTABILITY OF TUMORS INDUCED BY THE BB/T2 STRAIN OF POLYOMA VIRUS. (E.) Gimmy, J. (Inst. Med. Biol., German Acad.

Sci. Berlin, Berlin-Buch) and A. Graffi. Arch. Geschwulstforsch. 20(1):1-21, 1962.

After homologous s.c. or i.m. transplants to adult animals of tumors induced by the BB/T2 strain of polyoma virus in 2-day-old rats, mice or hamsters, tumor incidences were: in hamsters, 8/11, with an av. latent period of 65 days; in rats, 15/47, after an av. of 162 days; and mice, 1/5, after 85 days. In the case of hamsters, rats, and mice, after 21, 4, and 4 succeeding generations, the mean latent period was 36, 55, and 133 days, resp. There was no relationship between the percentage of successful takes and the length of the latent period; but transplantability varied considerably between histological tumor types. In some cases, particularly after extremely long latent periods (167-810 days), heterotopic and histologically different tumors appeared after s.c. or i.m. implantation of sarcomas induced by BB/T2 virus. These included pulmonary carcinoma, sarcoma of the liver, thyroid carcinoma, etc.; and were believed to be due to virus carried over with the inoculum of tumor tissue. Occasionally, especially with renal sarcoma, there was some deviation in structure, generally in the direction of increasing cellularity and polymorphism; these changes were believed to be an indication of increasing tumor malignancy.

63-501 IN VITRO CULTIVATION OF RAT SARCOMA XC CELLS CONTAINING ROUS VIRUS. (E.) Simkovič, D. (Inst. Oncol. Res., Bratislava, Czech.), N. Valentová and V. Thurzo. Folia Biol. (Praha) 8(4):221-229, 1962.

Cells of XC, a transplantable tumor obtained by Svoboda from a rat inoc. with Rous sarcoma virus (RSV) during the prenatal period, have produced Rous sarcoma-like tumors in chicks after 3 yr. of rat passage, although infectious RV has not been isolated, suggesting that the virus is carried in an integrated, non-infectious form. In the present study, short term attempts at in vitro cultivation of the tumor were successful, when cultures were grown on collagen, or in monolayers after an initial period of growth on collagen. Some of the tumor cultures appeared to adapt to long term in vitro growth, and one of these, XCTC 29 was studied in detail. Inoc. of $1-5 \times 10^5$ cells of XCTC 29 (culture age 12-30 days) s.c. into the wing of chicks caused RS in 19/27 animals, following a latent period of 9-20 weeks. Inoc. of $6-10 \times 10^5$ cells of an XCTC 29a-Tr substrain caused tumors in 5/19 chicks after a lag of 11-32 weeks (culture age 97-141 days). The supernatant from the growth medium of all of these cultures failed to show any evidence of RSV when inj. into chicks. After 30 and 98 days of cultivation, cells of XCTC 29a were implanted into newborn rats in doses of 5×10^5 cells/rat. Typical sarcomas grew in 20/21 animals inoc. with the parent strain, and in 18/19 animals inoc. with the Tr substrain. Lags were 4-5 days for the first, and 12-14 days

for the second tissue culture line. One of these rat tumors was cultivated again on collagen, and then the cell free medium was inoc. into chicks, which developed typical RS in 7/7, after a lag of 10-14 days. Repeated tests have failed to show RSV in short term cultures of other XC tumors.

- 63-502 THE KARYOLOGICAL AND HISTOLOGICAL CHARACTER OF INDUCED RAT TUMOUR XC PRODUCING ROUS VIRUS. (E.) Landa, Z. (Inst. Exp. Botany, Acad. Sci. CSSR, Prague), J. Svoboda and J. Jirásek. Folia Biol. (Praha) 8(1):12-15, 1962.

Tumors LVII and XC which developed in rats inoc. with Rous chicken sarcoma immediately after birth, were both epithelioid. The XC tumor, during passage in rats, became transformed to a spindle cell sarcoma with local angio-sarcomatous differentiation; transferred to chicks, typical Rous sarcoma of fowls was formed. Analysis of the XC tumor showed a rat karyotype.

- 63-503 STUDY ON THE HEMAGGLUTININATING ACTIVITY OF THE VACUOLATING VIRUS SV40. Irino, S. (Dept. Int. Med., Okayama U., Japan). Gan no rinsho (Jap. J. Cancer Clin.) 9(2): 84-87, 1963.

Hemagglutinating activity of the vacuolating virus SV40 against RBC of guinea pig was strongly positive (titer 1:16) and was inhibited by anti-rabbit serum (titer 1:320). Slight activity was shown against the RBC of the mouse, rat and sheep, but not against those of the chick, hamster, rabbit and human. The hemagglutinating activity of SV40 was inactivated by heating at 56°C for 30 min. The difference in the hemagglutinating activity between SV40 and polyoma virus is discussed.

- 63-504 ANAEMIA ASSOCIATED WITH THE NK/LYMPHOMA IN MICE. (E.) Davies, A. J. S. (Roy. Cancer Hosp., London, S. W. 3), A. M. Cross and K. Lapis. Brit. J. Cancer 16(4): 770-781, 1962.

In a study of the anemia associated with NK/lymphoma, CBA mice were inj. with the serum or RBC of tumor-bearing CBA mice and hematological changes were followed at intervals from 1 hr. to 24 days. Both serum and washed RBC caused anemia; in an incomplete experiment, the agent has been passaged every 7 days by means of inj. of 0.1 ml of serum without loss of infectivity up to the 30th passage. Absorption of serum from anemic mice with normal washed RBC did not abolish the capacity of the serum to produce anemia. When the agent was assayed by inj. of 0.1 ml of the agent-containing serum, and the infective titer was determined over a period of 14 days, the pattern of

multiplication was what might be expected of a virus. The infective agent was virtually completely inactivated at 56°C and with ether. Results of attempts at transfer of infection to other mouse strains were equivocal: either C3H, BALB/c, C57 BL and Swiss mice are less susceptible to attack, or the agent has specific growth requirements. It appears that the anemia is caused by a replicating agent which can be obtained free from the tumor cells; experimental evidence strongly suggests it is viroid in nature.

- 63-505 EXTRACHROMOSOMAL TRANSFER OF TUMOR CHARACTERISTICS; EFFECT OF FOSTER-NURSING ON THE BIOLOGIC AND MORPHOLOGIC BEHAVIOR OF MAMMARY TUMORS IN MICE. (It.) Squartini, F. (Inst. Anat. Path. Hist., U. Perugia, Italy), G. Rossi and I. Paoletti. Lavori Ist. Anat. Univ. Perugia 22(3):203-211, 1962.

C3H and BALB/cf mice with mammary tumor agent (MTA) (spontaneous in C3H, induced in BALB/c by foster-nursing with C3H mothers) showed the following mammary tumor characteristics: incidence 91.4% and 93.2%; time of appearance 320 and 277 days; short clinical duration (49 and 59 days) with a fast rate of growth (0.238 and 0.231 cm/week) which was regular in character; few partial regressions (27% and 34%); little or no dependence on pregnancy; a pure morphologic type and origin from nodules. The RIII strain which contains its own MTA showed different characteristics including an incidence of 73.7%, median latent period of 301 days, a long clinical duration (103 days) with slow rate of growth (0.135 cm/week), irregular growth, frequent partial regressions (59%) and dependence on pregnancy (80.3%), a varied morphology, and origin from plaques. In RIII mice, tumor incidence was 31.6%, 52.5% and 76.9% resp., in virgin, normally mated and force-mated females. In RIII mice foster-nursed by BALB/cf mothers, the clinical duration (62 days), rate of growth (0.218 cm/week), incidence of partial regressions (29.7%), incidence of tumors showing regular growth (78.4%), pregnancy dependence (14.3%), morphology and histologic origin were nearly identical to those of the foster mother strain. When BALB/cf mice were foster-nursed by RIII mothers, tumor incidence was 82% and 89.5% in normally and force-mated mice, resp. Tumor characteristics were those of the foster-mother strain. BALB/cf mice foster-nursed by C3H mothers showed tumor characteristics of the foster-mother strain. Male BALB/cf mice foster-nursed by RIII mothers have a high incidence of leukemias (48.3%), while females were found to have leukemias in 10.3%; the incidence for the parent strain is 0/25 for males and 1/46 for female BALB/cf.

- 63-506 THE DEFECTIVENESS OF ROUS SARCOMA VIRUS. (E.) Hanafusa, H. (Virus Lab., U. Cal., Berkeley), T. Hanafusa and H. Rubin. Proc. Nat. Acad. Sci. USA 49(4):572-580, 1963.

ocul of chick embryo cells, transformed by high filter Rous sarcoma virus (RSV) made free from Rous-associated virus (RAV), produced no RSV on repeated transfer. Such non-producing (NP) cells were morphologically Rous sarcoma cells, but sonic vibration and X-irradiation could not cause the release of virus. Infection of NP cells with RAV, however, (5×10^7 infectious units) resulted in abundant release of RSV within one day. RSV was never produced in the absence of RAV and was always initiated (in NP cells) in superinfection with RAV. Further experiment showed the absence of RSV production in the early stages of solitary infection. An inoculum of 100 FFU of RSV produced 6160 foci in 4 days, but only 238 when irradiated (probably from contamination with RAV). A similar inoculum plus 10^7 infectious units of RAV produced 7400 foci in 4 days, 7300 when irradiated. The ability of RAV to initiate RSV production was duplicated by all the viruses of the avian leukosis complex tested, including a visceral lymphomatosis virus (RIF), myeloblastosis virus, and an RAV-like agent isolated from standard RSV. It is concluded that the high filter strain (and probably the standard strain as well) of RSV virus is a defective virus, incapable of producing infective progeny in a solitary infection, and that RAV plays the role of a helper virus when multiplying in the same cell. Both capacities are perpetuated, in a cell line, by hereditary transmission. A possible relationship is suggested between the effectiveness of RSV and its carcinogenic properties. The failure to produce mature virus could result in unrestrained production of the early virus products, thus impairing the regulatory functions of the cell.

63-507 CANCER INDUCTION IN HAMSTERS BY HUMAN TYPE 12 ADENOVIRUS. EFFECT OF ROUTE OF INJECTION. (E.) Yabe, Y. (Baylor U. Coll. Med., Houston, Texas), L. Samper, G. Taylor and J. J. Trentin. Proc. Soc. Exp. Biol. Med. 113(1):221-224, 1963.

Human adenovirus, type 12, prototype strain (TCID₅₀ $\times 50$, after intrapulmonary (IPU), intrapleural (IPL), and i.p. inj. into newborn hamsters within 24 hr. of birth produced tumors at the site of inj. in 33-77 days; after s.c. inj., 0/3 had not developed tumors 508-636 days after inj. At minimum TCID₅₀ $\times 500$: after s.c. inj., 3/3 developed tumors within 37-98 days; IPL inj., 6/6 in 29-45 days; IPU inj., 4/5 in 42-45 days; i.v. inj., 2/3 in 50-70 days; intranasal instillation, 0/7 in 9 mo. Of 25 hamsters inj. intracranially, with minimum TCID₅₀ $\times 2-200$, abdominal tumors developed in 7/7 at the highest dose, with no tumors developed at the site of inj. Hydrocephalus developed in 3 of those inj. intracranially after 36-58 days. Of 35 hamsters with tumors at the site of inj., remote tumors of similar histology appeared in the liver of 10. Liver tumors were found in 4 i.v. inj. hamsters with

no tumor at the site of inj. at doses of minimum TCID₅₀ $\times 100$, 500, and 1,000. Some of the remote tumors are believed to be distant primary tumors. The fact that tumors appear at many sites of inj. indicates a wide dissemination of susceptible cells in the body.

63-508 IMMUNOLOGICALLY PRIVILEGED SITES IN STUDIES OF POLYOMA TUMOR ANTIGENS. (E.) Habel, K. (PHS, NIH, Bethesda, Md.) and J. H. Belcher. Proc. Soc. Exp. Biol. Med. 113(1):148-152, 1963.

Various types of tumor cells were inoc. into mice by various parental routes. Isologous transplants of mouse polyoma tumor 695 cells were inj. into C57BL/6 Jn female mice 4-8 weeks old; males were inoc. intratesticularly (IT). The number of inoc. 695 tumor cells required for tumors to take by various routes was: s.c. 10^4 ; s.c. with trauma 10^2-10^3 ; i.m. 10^4 ; intracerebral (IC), intraocular (IO) and IT 10^2 . The number of inoc. polyoma tumor 1923 cells required for tumor takes when isologous transplants were made to C57BL mice was: IC 10^2 ; s.c. 10^4 . C57BL Mice which received 400 r whole body irradiation showed an increased number of tumor takes compared to controls. When polyoma virus-immune C57BL mice were challenged by IC, IT or s.c. inj., the demonstrable resistance was 10^5 , 10^4 and 10^1 minimal transplantable number of cells, resp. This resistance is believed to be on a specific immunological basis. Mice immunized by a single dose of X-irradiated cells by IC or s.c. inj. of polyoma tumor 1923 cells showed no resistance in the s.c. immunized group and a ten fold degree of resistance in the IC immunized group. Attempts to produce tumors by inoc. of polyoma virus into immunologically privileged sites of C3H/He mice have failed to produce results.

63-509 GROWTH OF NORMAL AND ROUS SARCOMA VIRUS-INFECTED CHICK EMBRYO CELLS IN RAT BRAINS. (E.) Scotti, T. M. (U. Miami Sch. Med., Coral Gables, Florida), M. Dorsey, Jr., S. S. Lefkowitz, A. Duwelius and M. M. Sigel. Cancer Res. 23(4):531-534, 1963.

Exposure of 10^5 , 10^6 , and 10^7 trypsin-dispersed chick embryo cells to Rous sarcoma virus (RSV; infectivity titer adjusted to 10^{-2}) for 15-90 minutes before intracerebral inj. into rats conditioned by x-irradiation and cortisone, produced Rous sarcomas in 10/16, 16/19, and 17/19, resp.; 10^7 uninfected trypsin-dispersed cells produced small collections of cells admixed with collagen fibers in 5/9 after similar inoc. Exposure of 10^5 and 10^6 tissue culture chick embryo cells to RSV for 15-30 minutes before inoc. initiated growth of Rous tumors in 1/3 and 4/5, resp.; 10^6 uninfected cells survived in 2/6. More abundant growths were often obtained when cells were exposed to virus for 2 days prior to inoc. All Rous tumors were microscop-

ically identical regardless of time of exposure to RSV or trypsinization. The infected cells gave no evidence of transformation by RSV at the time of inoc. Hemorrhages appeared in many Rous tumors.

63-510 THE METABOLISM OF MOUSE EMBRYO CELLS GROWN IN VITRO AND INFECTED WITH THE ONCOGENIC VIRUS SE POLYOMA. (E.) Guminska, M. (Med. Sch., Krakow, Poland), B. Skarzynski and Z. Porwit-Bohr. *Acta Biochim. Pol.* 10(2): 163-171, 1963.

Endogenous respiration and aerobic glycolysis were measured in cultures of Porton strain mouse embryo cells (70×10^5 cells av.) 48-hour-old when infected with 10^5 TCID of SE polyoma virus. The release of virus into the medium was preceded by a decrease in endogenous O_2 consumption (1 day after infection $10.8 \mu\text{l}$ per hr. per mg dry wt. as compared with uninfected controls, $15.8 \mu\text{l}$) and an increase in lactic acid production; respiration was lowest 6 and 7 days after infection ($0.8 \mu\text{l}$ infected cells, $7.2 \mu\text{l}$ controls) just prior to appearance of the cytopathogenic effects and at the highest titer of virus. Surviving cells on the 9th day showed greater respiration than during cytopathogenesis. The Crabtree effect was greater in infected cells except those surviving cytopathogenesis (45% decrease in O_2 consumption in infected cells, 33% decrease in controls).

63-511 STUDIES OF LEUKEMIA L₂C IN GUINEA PIGS. (E.) Jungeblut, C. W. (Lenox Hill Hosp., New York) and H. Kodza. *Arch. Ges. Virusforsch.* 12(4):537-551, 1963.

Leukemia L₂C was found to be transmissible, in routine passages, with the supernatants of high speed centrifuged leukemic spleen extracts, and of leukemic plasma harvested at early and late stages of the disease. The same agent was transmitted with leukemic spleen extracts, brain extracts, or sera after the materials had been passed through bacteria-retaining filters of various types. Susceptibility to the L₂C agent appears to be limited to inbred strain 2 guinea pigs or to F1 hybrids from crosses of susceptible and resistant guinea pigs, suggesting that susceptibility is inherited as a dominant characteristic. The leukemogenic agent is capable of passing the placenta, and tissues from normal appearing embryos of leukemic mothers may be shown to harbor the agent. When inj. i.p. into susceptible guinea pigs, the leukemogenic agent appeared in the plasma at 4 days and was present in all subsequent samples. Whole blood transmitted leukemia at 24 and 48 hr., but not at 72 hr. Beginning at 4 days, all subsequent blood samples again transmitted the disease. In the resistant animals, the leukemogenic agent could be detected sporadically during the first 5 days in plasma or in whole blood, but not after that time.

63-512 INTERFERENCE BETWEEN LYMPHOCYTIC CHORIOMENINGITIS VIRUS AND THE LEUKEMIA TRANSMITTING AGENT OF LEUKEMIA L₂C IN GUINEA PIGS. (E.) Jungeblut, C. W. (Lenox Hill Hosp., New York) and H. Kodza. *Arch. Ges. Virusforsch.* 12(4):552-560, 1963.

A wild strain of lymphocytic choriomeningitis virus (LCM) was isolated as a "passenger contaminant" from hybrid guinea pigs inoc. with leukemia L₂C. Infection with this strain of LCM virus significantly increased the life span of guinea pigs infected with cell free leukemic material by delaying appearance of the leukemogenic agent in the plasma of the animal. Leukemic guinea pigs, inj. with LCM virus from a highly pathogenic mouse or guinea pig strain, or from a nonpathogenic tissue culture strain, tolerated the virus for long periods of time without ill effects. The LCM agent could be separated from the L₂C agent by filtration. The data suggest that LCM virus and the leukemia-transmitting agent form an interference system which is capable of operating under both natural and experimental conditions of infection. The interfering effect of LCM virus appears to be dependent upon the multiplying virus particle, and no evidence has been found for an interferon-like substance. Admin. of a more potent virus, like Col SK virus, did not add to the sparing effect of LCM virus, perhaps because the pronounced lymphotropic properties of LCM virus in the guinea pig have a bearing on its marked anti-leukemic propensities.

63-513 EXPERIMENTAL INVESTIGATIONS IN HUMAN LEUKEMIA ATTEMPTS AT TRANSMISSION TO THE HYBRID WHITE MOUSE. (E.) Nastac, E. (Inst. Infamicrobiol. R. P. R. Acad., Bucarest), B. Anagnoste, G. Balmus and D. Tărchilă. *Neoplasma (Bratisl.)* 10(1):61-64, 1963.

Blood and sternal marrow from 5 pts. with chronic lymphatic leukemia during the acute phase were inj. by s.c., intramedullary, intracerebral and i.v. routes into white adult hybrid newborn, and newborn AKm mice. About 25% of mice inoc. intracerebrally with material from 1 pt. showed an increase in WBC to 108,000 with 11% myelocytes at about $3\frac{1}{2}$ mos., whereas material from 3 other pts. caused no apparent change in WBC. When material from a 5th case was inoc. i.v., 4/10 mice were alive at 6 mos., 3 presented an increase in WBC (48,000-57,000) at 9-12 mos., and 1 an increase in the number of WBC (56,800), a hepatic tumor, ascites, lung tumor, hypertrophy of lymph nodes and splenomegaly at 11 mo. After serial passage (up to the 5th) of liver or spleen from animals that died of the experimental disease, there resulted in recipients alterations of the leukocyte formula, death after about a 2-weeks latency, and lymphoid infiltrative lesions of the liver, spleen and lymph nodes.

See also abstract nos.: 348,350,364,382,405, 447

EPIDEMIOLOGY AND BIOMETRY

514 WORLD INCIDENCE AND DISTRIBUTION OF SKIN CANCER. (E.) Segi, M. (Dept. Health, Tohoku U. Sch. Med., Sendai, Japan). Nat. Cancer Inst. Monogr. (10):245-255, 1963.

Although it is pointed out that the mortality from skin cancer is relatively low, so that mortality data are of limited usefulness in studying its geographical distribution, the author presents data on the age adjusted death rates of skin cancer in 24 countries over the period 1950-59. Particularly high rates for 1958-59 are noted in South Africa (3.61), Australia (2.88), New Zealand (2.71) and Ireland (2.75), with very low rates in Japan (0.97) and for non-whites in the USA (1.15). The death rate generally seems to be falling in the older age groups and rising in the younger, with a consistent male:female sex ratio of about 1.2:1.7. On a worldwide basis, there is a negative correlation between the incidence of skin cancer and that of gastric cancer, while in Japanese males, the frequency of skin cancer is positively correlated with the mean annual hr. of sunshine. Data on cancer by site shows that skin cancer represents an appreciable proportion of all new cancers in countries surveyed. Again, relative to all cancers, incidence was found to be high in New Zealand (23.1%) and the USA (Caucasians) (16.7%) and very low in Japan (0.6%).

515 SKIN CANCER IN AUSTRALIA. (E.) ten Seldam, R.E.J. (Dept. Path., U. Western Australia Med. Sch., Perth). Nat. Cancer Inst. Monogr. (10):153-166, 1963.

Among 11 countries (including Japan, USA, Ceylon, Israel, Canada, The Netherlands, Scotland, Denmark, S. Africa), Australia has the highest death rates from malignant melanoma (19.1) and from all skin malignancies (34.5). For all skin cancers, age-corrected death rates rise sharply for both sexes after age 60. The commonest skin cancers between 1957-1960 (per million) were basal-cell carcinoma (1116) and squamous-cell carcinoma (111), with 93.23% of the lesions occurring on the head, neck and upper limb. Incidence increased with age from 25 cases under age 30 to 711 over age 70, with highest incidence in males. Actinic keratosis presented patterns of high incidence, site, and sex distribution similar to those of squamous-cell carcinoma, which suggests common etiological factors. The strong sunlight, high annual distribution of sun-hours and high temperature with tendency for outdoor activity were considered prime factors in malignant melanoblastoma, especially among fair-skinned people.

516 ALBINISM, XERODERMA PIGMENTOSUM, AND SKIN CANCER. (E.) Keeler, C. E.

(Milledgeville State Hosp., Ga.). Nat. Cancer Inst. Monogr. (10):349-359, 1963.

Based mainly on his experience with albinism among the Caribe Cuna Indians of San Blas (Lower Panama), the author contrasts the symptomatology, histology, treatment, prognosis and heredity of xeroderma pigmentosum and albinism, and emphasizes the high incidence of skin cancer associated with these conditions in a tropical environment. Albinism and xeroderma pigmentosum are similar in their cutaneous symptoms and recessive heredity (although the gene for xeroderma may be partially sex-linked), and the incidence of each is about 1 in 10,000 except in highly inbred groups such as the Cuna Indians where the incidence of albinism is 0.45%. Compared to the temperate zone, the incidence of xeroderma pigmentosum is low in the tropics (about 1/20,000); neoplasms that occur include basal-cell, squamous-cell and sometimes spindle-cell carcinomas. Among albinos, skin cancers (usually squamous-cell carcinomas) were found in albinos in their teens or early twenties; metastatic cancer eventually represented the major cause of death.

63-517 INFLUENCE OF AGING ON THE SKIN. (E.) Cowdry, E. V. (Jewish Hosp. St. Louis) Nat. Cancer Inst. Monogr. (10):335-348, 1963.

In a general discussion of the relationships between aging and cancer, it is pointed out that the age of maximal prevalence varies from 0-4 yr. for renal and adrenal tumors up to 60-65 yr. for skin cancer and over 70 yr. for carcinoma of the prostate; the concept of latency and the attempts which have been made to measure the latent periods for human cancers is then discussed. In a review of biochemical studies on mouse epidermis during the induction of squamous-cell carcinoma with 20-methylcholanthrene, it was shown that certain cellular constituents, like lipid phosphorus, succinic dehydrogenase, ATPase and some amino acids increased markedly during the latent period, while others were unchanged and still others, such as calcium and other cations, non-protein nitrogen, ammonia, urea and biotin, decreased. Also discussed, was the initiation and promotion stages of cutaneous carcinogenesis and the role of the dermis; it was concluded that there was evidence for the idea that cancer runs a milder course in older pt., the individual cell and possibly the organism as a whole becoming more resistant to cancer with age; on the other hand, the age factor may be overruled by many other variables.

63-518 CHEMICALLY INDUCED SKIN CANCERS IN MAN. (E.) Hueper, W. C. (NCI, Bethesda). Nat. Cancer Inst. Monogr. (10):377-391, 1963.

After pointing out the special place occupied by cancer of the skin and the chemicals which cause

it, a review (48 references) of the literature is presented dealing with the polyetiology of chemically-induced skin cancer (a variety of carcinogens combined with sunlight, chronic irritation and other factors), the complex of precancerous and pericancerous symptoms produced by contact with chemical carcinogens, some of the epidemiological data on skin cancer with information classified by site, social class and occupation, and the influence of type, site and intensity and duration of exposure (the question of the latent period). He emphasizes that chemically-induced skin cancer is not only of historical interest but is important as the most common and accessible prototype of all environmental cancers with respect to etiology, epidemiology, diagnosis, symptomatology, pathology and control. In fact, chemically-induced skin cancer is probably even more common than generally reported, and should be taken as a warning in any particular case that the chemical concerned probably has carcinogenic activity for other organs as well.

- 63-519 SOME ETIOPATHOLOGIC ASPECTS OF SKIN CANCER IN SOUTH VIETNAM. (E.) Pham Bieu Tam (Saigon Fac. Med., South Vietnam), Dao Duc Hoanh, Nguyen Xuan Chu and Nguyen Huy Can. *Nat. Cancer Inst. Monogr.* (10):75-79, 1963.

Among 281 cases (127 male, 154 female) of skin cancer in South Vietnam treated between 1955 and 1960, 80 women and 10 men had cancer of the lip, with onset in the middle to older age group (40-85 yr.). Of the 80 women, only 23 were outdoor workers, 30 were indoor workers and 18 had no work, indicating that tobacco chewing or smoking and a condition resembling the Plummer-Vinson syndrome may be more important etiological factors than sunlight. Genital cancer (87 penile and 48 vulval cancers) seems to begin earlier in life; 90% of all pts. with penile cancer had phimosis, and vulval cancer seemed to be favored by multiparity and syphilis. Of the 56 pts. with cancer of the exposed skin, 48.5% were laborers and 25.3% were outdoor workers, indicating sunlight as an etiological factor; however, only 20% of the lesions were in exposed areas, so that other factors must be considered. Histologically, squamous-cell carcinoma was the most common (55.5%); malignant melanomas were relatively rare.

- 63-520 CLINICO-PROGNOSTIC EVALUATION OF CUTANEOUS MELANOMAS. PART III. (Conclusion). (Sp.) Amoretti, A. R. (Dermosyphil. Clin., U. Montevideo, Fac. Med., Uruguay). *An. Fac. Med. Montev.* 47(3-4):157-172, 1962.

The usefulness of the classification of melanomas according to their origin (and hence their malignancy) is here exemplified in an analysis of 50 pts. (22 male, 28 female; age range, 23-105). In 50%, the melanomas developed from nevi; in 32%, from malignant lentigines; and 18% were primary skin melanomas. Nevus-derived melanomas occurred in almost all age groups, most frequently at age

41-50, whereas melanomas deriving from malignant lentigines were most frequent at age 71-80. Primary skin melanomas were not observed in subjects under 50. The sites most frequently affected were the face (28%), trunk (22%), and the sole of the foot (20%). Before age 50 the main site of melanomas was the trunk; all of the facial and plantar melanomas appeared after this age. In women, melanomas of the face and lower extremities were most frequent; in men, melanomas of the trunk (all developing from nevi) predominated. Melanomas originating in malignant lentigines appeared at all sites except the trunk, over half of them on the face. Eight of the 9 primary melanomas were located in the plantar region, the other was on a leukodermic area of the leg. In discussing the pathogenesis of melanomas, the author emphasizes the role of recurrent trauma -- although 8 of the 25 cases of nevus melanoma developed after a single trauma. The relatively greater exposure of the male torso to trauma may account for the greater frequency in this sex of melanomas of this region; the greater exposure of the female legs to trauma (including repeated shaving and application of depilatories), for the greater frequency of melanomas of the lower limbs in women.

- 63-521 A STUDY OF TWENTY-ONE INSTANCES OF AMELOBLASTOMA, A TUMOR OF ODONTOGENIC ORIGIN. (E.) Gardner, A. F. (U. Maryland School Dent., Baltimore), M. B. Apter and J. H. Axelrod. *J. Oral Surg.* 21(3):230-237, 1963.

The literature on ameloblastoma is reviewed. In the cases reported here (from Baltimore hospitals) this benign jaw tumor occurred over a wide range of ages (17-71, mean at diagnosis 43 yr.); 7/21 were males, 8/21 were Negro (not significant); 20/21 were situated in the mandible. The mean duration (since detection) was 6.4 yr., mean dimensions of excised tumor 5 x 4 cm. Incidence was not clearly related to occupation; most prevalent occupation was that of housewife. The majority of pts. were in a low socioeconomic group. The origin of ameloblastoma has been ascribed to trauma, but the more probable theory is the one which attributes its origin to epithelial cell rests.

- 63-522 CARCINOMA OF THE STOMACH. (E.) Gangadharan, D. (Dept. Path., Andhra Med. Coll., Visakhapatnam, India) and D. B. Reddy. *Indian J. Path. Bact.* 5(2):80-92, 1962.

Analysis of autopsy records (1926-1960) and biopsy records (1951-1960) from Visakhapatnam, India, showed 55 gastric carcinoma cases at autopsy and 49 resected gastric cancers. The 55 gastric carcinomas constituted 1.9% of the 2916 autopsies and 15.2% of the 363 malignancies found, suggesting that stomach cancer is more prevalent in some regions in India than had been supposed. As to age distribution, 43 (40%) of the pts. were 40-49 yr. old; 75% were under 50. Male to female ratio was 5:1. All the pts. were in a low income group.

etary deficiency might be an etiologic factor. The most frequent site of gastric carcinoma was the stomach (60%) and ulcerative lesions were most frequent (70%). Adenocarcinoma was the most common histologic type (59%). One ulcer-cancer was encountered.

523 REGIONAL STUDIES IN SKIN CANCER. FIRST REPORT: NORTH-WESTERN QUEENSLAND. (E.) Verstone, H. (Dept. Social Prev. Med., U. Queensland, Australia), C. B. Campbell, C. S. King, L. P. Lang and R. G. Richardson. Med. J. Aust. 1(9):312-315, 1963.

Results of a house-to-house survey and personal examinations of 284 men and 210 women over 40 yr. of age who had either been born or had lived in northwest Australia (dry tropical climate) for over 30 yr. (probably representing 82% of all the eligible adults in the 2 counties considered) showed that 166 males and 89 females had some type of skin lesion; these included keratotic lesions (1253 in 153 males, 520 in 82 females); and skin cancers (47 in 32 males, 30 in 20 females). The incidence of both types of lesions increased with age: for keratoses maxima 63-67% occurred at 50-70 yr. in men; and 56-63% at age 60 to over 70 in women. Maxima for skin cancer of 19%-21% occurred beyond age 60 in both groups. The incidence of cutaneous lesions was significantly higher in subjects who lived easily in the sun compared to those who lived readily; similarly, the incidence of keratosis was 32.6% and 48% in dark complexioned women and men, compared to 49.4% and 67% in light complexioned women and men, resp. The prevalence of both keratosis and skin cancer was also 2-3 times higher in men with outdoor occupations as in those leading primarily indoor lives. The incidence of skin cancer, in turn, was 4.6-4.7 times higher in pts. with keratosis as in those without. In the men, 33.2% of the keratotic lesions and 90% of the cancers occurred on the face and neck, 65.7% of the keratotic lesions and 10% of the cancers appearing on the hands and arms. The above data indicate a definite correlation between skin cancer and exposure to sunlight.

524 ORAL AND PHARYNGEAL CANCER IN INDIA. (E.) Paymaster, J. C. (Tata Mem. Hosp., Bombay, India) and P. Gangadharan. CA 13(2):71-72, 1963.

In India 35% of all cancer occurs in the oral cavity or pharynx. Among possible precancerous conditions observed by the authors were: leukoplakia (32%) and localized fibrosis affecting the tongue and hard palates, the tonsillar fossae and, less frequently, the buccal mucosa. The fibrosis is progressive, leading ultimately to trismus and atrophy of the soft palate; carcinoma developed in 30% of such cases. From an analysis of hospital records it is seen that oral carcinoma frequently increases, and oropharyngeal and hypopharyngeal carcinomas decreases as one moves southward. The

increase is primarily in cancers of the buccal mucosa. In South and West India it is customary to chew pan (a preparation of tobacco, betel leaf and nut, slaked lime, and spice) which is held in contact with the oral mucosa for hr. at a time. In other areas, where carcinomas of the oropharynx and hypopharynx predominate, smoking of bidi (tobacco rolled into a small leaf from a tree of the ebony family), is common. A high frequency of carcinoma of the palate was observed in Andhra Pradesh, where adda poga (smoking the lighted end of a cigar), has been reported. See also CRA 1(2):293, 1963.

63-525 CANCER OF THE BUCCAL CAVITY AND NASOPHARYNX IN SINGAPORE. (E.) Muir, C. S. (Dept. Path., U. Singapore). Brit. J. Cancer 16(4):583-591, 1962.

During 1954-58 cancer of the buccal cavity and nasopharynx in Singapore constituted 8% of all cancers; in Connecticut (1955-6) they constituted 3.3% of all cancers, in England and Wales (1957), 4.2% of all cancers. Mortality rates (as reported by WHO) were (1952-56): Singapore, 7.3% (of all cancer deaths), Japan and Israel 0.9%, England and Wales, and U.S. (whites) 2.3%, U.S. non-whites 2.1%, Australia, 2.2%. In Singapore, death from pharyngeal cancer is highest between the ages of 40 and 50 for both sexes. Nasopharyngeal cancer in other parts of the Far East is also reviewed.

63-526 REMARKS ON CARCINOMAS AND PRECANCEROUS CONDITIONS OF THE SKIN. (Ger.) Fischer, W. (Dermat. Clin., U. Geneva). Dermatologica (Basel) 126(3):188-204, 1963.

After the accidental discovery of apparently familial skin cancer in 15 pts. belonging to 5 families treated at the author's clinic (brother and sister pairs with either carcinoma or precancer, plus the father and mother in 1 case and a paternal cousin in another), 150 skin cancer pts. were questioned as to the occurrence of skin cancer among their relatives. This survey revealed 2 definite instances of familial incidence (1 pt. with clinically diagnosed precancers in the father, mother and 2 daughters; and another with histologically diagnosed precancer or intermediary carcinoma in 2 cousins), and 13 doubtful cases (relatives not available for examination). This is compared with data from the literature. A statistical evaluation is presented of 783 pts. (392 men and 391 women) with histologically diagnosed skin carcinoma (490 cases, including 244 men and 246 women) or precancerous conditions. The 490 carcinomas included 124 spinocellular carcinomas (65 in men and 59 in women), 305 basal-cell carcinomas (151 in men and 154 in women) and 61 others. In the over-all group of 1198 pts. (415 diagnosed only clinically), as well as in those with histological diagnoses or those with carcinomas only, in both sexes, the highest incidence was in the 70-79 yr. age group, with the great majority between 50 and 80; this was true

of both men and women, only 16 women and 6 men with histologically verified carcinomas were below age 39. Finally, a study of the eye color in 150 pts. with carcinoma or precancer showed light colors in 62.7% and dark colors in only 28.7%, compared to 16% and 47.4%, resp. in controls without skin cancer; this is felt to be a significant correlation, which favors the genetic transmission (familial incidence) of skin cancer.

63-527 CANCER IN NORTH VIETNAM IN COMPARISON WITH CANCER STATISTICS FROM THE GERMAN DEMOCRATIC REPUBLIC. (Ger.) Wildner, G. P. (Path. Inst., Humboldt-U., Berlin). Deutsch. Gesundheits. 18(7):290-296, 1963.

Among 46,486 cases (20,250 males, 26,236 females) of newly diagnosed cancer recorded in the German Democratic Republic in 1957, carcinomas (including basaloma, hypernephroma and seminoma) accounted for 18,139 male and 23,885 female cases, giving an incidence (per million) of 231.3 and 246.8, resp.; the comparable figures for sarcomas were 593 males (7.6) and 754 females (7.8). Among the males, the most frequent sites for carcinoma were the stomach, lung, skin and intestine; among the females, the most frequent sites were the uterine cervix, breast, stomach, skin and intestine. The sarcomas were mostly reticulum cell sarcomas, lymphosarcoma, osteosarcoma and connective tissue sarcoma, with the uterus and ovaries common sites in women. The over-all highest cancer incidence was at 65-70 yr. of age (also at 75-80 if the composition of the population was considered). Cancers of the breast, skin and stomach reached a maximum incidence at 60-80 yr., but cervical carcinoma appeared earlier, with a maximum at 40-50 yr., and sarcomas reached a maximum at 55-65 yr. A comparison of these statistics with those reported on the basis of pathological specimens from North Vietnam indicated for the Vietnamese a higher incidence of carcinoma of the penis, uterine cervix, upper respiratory tract, mouth and throat, liver and thyroid, chorio-carcinoma and sarcoma in general, and a lower incidence of carcinoma of the uterine body, ovary, lung, intestine and prostate. These differences are probably due as much to the different age distribution in the 2 populations as they are to specific dietary, cultural or geographic factors. (See also CRA 1(3):#532, 1963.)

63-528 REPORT ON THE STATISTICAL EVALUATION OF THE FINDINGS OF THE RHINE-WESTPHALIA PATHOLOGICAL SOCIETY WITH RESPECT TO BRONCHIAL CARCINOMA. (Ger., Abstract) Mittman, Kneller and Poche. Zbl. Allg. Path. 104(1/2):98-99, 1962.

A comparative evaluation of the 1,229 cases of bronchial carcinoma recorded in the Institutes of Pathology of 12 German cities in 1955-60 and the autopsy records in 3 of these cities for the previous 23-52 yr. showed that the incidence of bronchial carcinoma (predominantly squamous-cell and undifferentiated microcellular carcinomas) has increased in both men and women since the beginning of the century, the current incidence at autopsy

being about 10-14% versus only 0.5% in the first decade of this century; this increase is particularly marked in the age group just below 60 yr. An attempt to correlate the proportion of squamous cell carcinomas (which rises with the over-all incidence of bronchial carcinoma) with various environmental factors showed no correlation with changes in residence or occupation, and only a weak correlation with cigarette smoking (0.09), but a strong correlation with type of occupation; thus, persons working in the countryside, in factories and in commerce seem to be exposed to more environmental carcinogenic factors than office workers or housewives.

63-529 CONSIDERATIONS ON THE GATHERING OF MORBIDITY STATISTICS FOR CANCER. (Ger.) Schinz, H. R. (Zurich, Switzerland). Oncologia (Basel) 16(2):148-151, 1963.

After distinguishing between morbidity, mortality and lethality and pointing out the admitted value of such statistical information, the author reviews the requirements and problems in the collection of morbidity data. Since the number of cancer pts. at the end of any particular yr. is a function of many other variables (the number at the beginning of the yr., and the number of new cases, lost to follow-up, of relapses, cured, and the mortality), long-term, continuous records are required, with considerable invasion of privacy and the doctor-pt. relationship. The author points out that the lack of adequate diagnostic facilities and the absence of compulsory registration for cancer makes most morbidity statistics (usually calculated on the basis of hospital admissions) highly inaccurate. Finally, some specific applications of these questions to Zurich are discussed.

63-530 SKIN CANCER IN INDONESIA. (E.) Pringgoutomo, S. (Inst. Path., U. Indonesia Sch. Med., Djakarta) and S. Pringgoutomo. Nat. Cancer Inst. Monogr. (10):191-195, 1963.

Statistical analysis of surgical specimens from 526 pts. with skin cancer seen by the authors during the period 1955-1960 revealed 225 squamous cell carcinomas of the skin (143 males, 81 females, incidence increasing with age up to 31-40 yr.), 170 basal-cell carcinomas of the skin (91 males, 79 females, with the highest incidence in the 41-50 yr. age group), 103 malignant melanomas (63 males, 39 females, peak incidence at 41-50 yr. of age), 20 squamous-cell carcinomas of the penis (apparently all uncircumcised), 3 dermatofibrosarcomas and 5 senile keratoses. With regard to localization, 35% of squamous-cell and 65% of the basal-cell carcinomas were on the face, and only 17.6% of the carcinomas were on the lower extremities, representing a decrease compared to earlier studies. Of the malignant melanomas, 63 were on the lower limbs and 21 on the head and neck, also representing a shift away from the lower limbs. The authors suggest

that these shifts are due to improved hygienic conditions and increased wearing of shoes, particularly in women.

531-533 MALIGNANT MELANOMA OF THE SKIN IN MAN. (E.) Helwig, E. B. (Armed Forces Inst. Path., Washington, D.C.). Nat. Cancer Inst. Monogr. (10):287-295, 1963.

Among 392 pts. with malignant melanoma recorded at the Armed Forces Institute of Pathology (including 192 cases of cellular blue nevus), 323 were male, 96% were Caucasian and there were only 7 Negroes, in each of whom the melanoma involved the sole of the foot or the palm of the hand. The median age was 34 yr., which is higher than for the Armed Forces as a whole; 72% had blue, gray or green eyes, 60% had blond or red hair and almost 80% had fair or ruddy complexions. Among the Caucasians, 30% had melanoma on the trunk (including 76 lesions on the skin of the back), 25% on the lower extremities, 23% on the head and neck and 22% on the upper extremities; 10% of all pts. claimed origin of the melanoma in a preexisting nevus. A relationship between sunlight and melanoma was suggested by the fact that 183/287 Caucasian males had lived in states below or bordering on the 44th parallel. The prognosis and histological diagnosis of malignant melanoma are discussed. The author then points out that malignant melanoma in children behaves essentially the same as in adults, and that the term "juvenile melanoma" is inappropriate for the spindle cell and epithelioid cell nevi. Finally, among 192 pts. with cellular blue nevus, which is often mistaken for malignant melanoma but is much more benign, only 4 showed metastasis, and even in these cases only the regional lymph nodes were involved, no recurrence having been observed in any case 8-15 yr. after their excision.

532 TUMOR INCIDENCE IN NORTH VIETNAM. (Ger.) Troung Cam-Cong (Inst. Hist. Embryol., Med. Fac. Hanoi, Democratic Republic of Vietnam). Dtsch. Gesundh. 18(4):157-166, 1963.

Among 4,151 tumor sections representing 13,699 cases referred from hospitals throughout Vietnam for examination by the Radium Institute (Hanoi) between 1955-60, 2,473 (60%) proved malignant. Within this group, the percentage incidence of each tumor type was tabulated as follows: carcinoma, 84.2; sarcoma, 12.6; malignant urogenic tumors (chiefly, retinoblastomas), 1.8; chorioepithelioma, 0.8; malignant melanoma, 0.4; and malignant embryoma, 0.2. The most frequent carcinomas in males were those of the stomach (22.6%), stomach (17.3%), pharynx (12.0%), buccal cavity (10.0%), and liver and gall bladder (8.8%); in females, those of the cervix uteri (9.8%), breast (18.0%), buccal cavity (8.4%), stomach (6.1%), and pharynx (5.1%). Of all cancers the respiratory tract, the greatest incidence in both men and women was in the pharynx, these

were more than twice as frequent in the male. The incidence of sarcomas in men was approximately twice that in women; with those of the hematopoietic tissues accounted for 64.8% and 59.8% of the totals, resp.; those of the connective tissues and blood vessels accounted for 24.3% and 29.4%, resp. Reticulum cell sarcoma of the bones, myelosarcoma, and Hodgkin's disease were rare; the latter was seen in only 11 men and 1 woman.

63-533 MYCOSIS FUNGOIDES. (E.) Edgcomb, J. (NCI, Bethesda), J. Block, A. Eisen and E. Van Scott. Nat. Cancer Inst. Monogr. (10):275-280, 1963.

A total of 38 pts. with mycosis fungoides were observed for a period of 7 yr., during which time 21/38 died. The disease developed in most pts. at ages of 30-60 yr., and was preceded by nonspecific or psoriasiform dermatoses. In 22/38, diagnosis was made in the pretumor stage. Biopsy or autopsy in 22/38, revealed: dermatophic lymphadenopathy in 10/22; lymphosarcoma in 4; Hodgkin's granuloma in 1; reticulum cell sarcoma in 1; lymphoma in 6.

63-534 FOLLOW-UP STUDIES OF PATIENTS WITH SUPERFICIAL GASTRITIS AND PATIENTS WITH A NORMAL GASTRIC MUCOSA. (E.) Siurala, M. (2nd Med. Clin., U. Helsinki, Finland) and Y. Vuorinen. Acta Med. Scand. 173(1):45-52, 1963.

Upon reexamination of 43 pts. with superficial gastritis after an av. of 8.4 yr. after the original diagnosis, none showed signs of gastric tumor. Biopsy studies revealed that 13 had slight and 7 severe atrophic gastritis. Among 45 with normal gastric mucosa, after an av. of 9.5 yr., superficial gastritis had developed in 12, and a slight atrophic gastritis without metaplasia in 4. In a previously reported series, 7/116 pts. with atrophic gastritis progressed to gastric tumor.

63-535 PERSONALITY CHARACTERISTICS IN MALES CONDUCTIVE TO LUNG CANCER. (E.) Kissen, D. M. (Dept. Psycholog. Med., U. Glasgow, Scotland). Brit. J. Med. Psychol. 36(Pt. 1): 27-36, 1963.

Among 161 male lung cancer pts. interviewed or responding to a questionnaire (often before diagnosis of their disease had been made), fewer (26.1%) gave a history of childhood behavior disorders (e.g. bedwetting, temper tantrums) than among 174 male non-cancer pts. (41.4%). More of the cancer pts. (59.7%) admitted to a tendency to conceal or bottle up emotional difficulties than controls (42.8%). There was no correlation with amount of cigarette smoking, nor with lack of aggression or sociability, nor with tumor histology. There was a marked statistical correlation, however, with a low mean score for neuroticism (previously reported). The pts. tended to be somewhat extraverted.

- 63-536 CANCERS IN PATIENTS WITH TUBERCULOSIS OF THE LUNG. (Fr.) Collas, R., J. Peninou-Castaing and G. Marissal. Poumon Coeur 19(1):41-45, 1963.

Over a 5-year-period, 27 malignancies were discovered among 913 pts. near or over age 50 admitted to a sanatorium with confirmed tuberculosis, to give a cancer incidence of 3%. Most of the pts. with cancer and ulcero-caseous forms of tuberculosis; all smoked, 23 also drank. The cancers were discovered 6 mo.-14 yr. after diagnosis of TB, on the av. after 4 yr. 3 mo. Only 1 pt. was less than 50, 2 were over 70 yr. of age. In 21/27, the neoplasms were discovered after bacteriological examination had become negative, and in 23/27 after marked regression or disappearance of lung lesions. Distribution of the tumors by site was bronchi 9, larynx 5, tonsil 3, esophagus 3, 1 each pleura, maxillary sinus, tongue, thyroid, skin, vertebra, and prostate.

- 63-537 MORTALITY FROM CARCINOMA AND CARDIO-VASCULAR DISEASES IN PATIENTS WITH PARTIAL GASTRECTOMY FOR PEPTIC ULCER. DISCUSSION OF POSSIBLE RELATIONSHIP BETWEEN SIDEROPENIA AND DEVELOPMENT OF CARCINOMA. (E.) Holstad, H. A. (Ullevål Hosp., Oslo, Norway). J. Oslo City Hosp. 13(3):37-51, 1963.

To analyze the general over-mortality from cancer in partially gastrectomized ulcer pts., a follow-up study was made of 749 gastric or duodenal ulcer cases operated on from 1946 through 1958; 715 were observed for 2-14 yr. and 34 for less than 2 yr. Of the 55 deaths registered, 21 were due to cancers (19 carcinoma, 2 leukemia and pulmonary lymphogranulomatosis). Peak age at operation was 41-50 yr. (33.21%). Compared to the general population there were excess deaths in the sixth and seventh decades; the oldest and youngest groups were under-represented. Deaths from carcinoma, compared with the number expected in the general population, showed a more than three-fold increase for men and a more than two-fold increase for women. Malignant lesions of the respiratory tract predominated (43.75%), whereas in the general population g.i. tract lesions usually predominated. Among the 19 pts. who died of carcinomas, 14 showed anemia and 10 degenerative epithelial changes. The correlation between development of carcinoma and occurrence of hypochromic anemia and/or epithelial changes in this series was so definite that a causal relationship could not be excluded.

- 63-538 STUDIES ON THE EPIDEMIOLOGY OF MYXOMATOSIS IN CALIFORNIA. I. OBSERVATIONS ON TWO OUTBREAKS OF MYXOMATOSIS IN COASTAL CALIFORNIA AND THE RECOVERY OF MYXOMA VIRUS FROM A BRUSH RABBIT (SYLVILAGUS BACHMANI). (E.) Marshall, I. D. (Dept. Microbiol., Australian

Natl. U., Canberra, A.C.T.), D. C. Regnery and G. Grodhaus. Am. J. Hyg. 77(2):195-204, 1963.

Strains of myxoma virus recovered for the first time from a naturally infected brush rabbit (Sylvilagus bachmani), from 2 pools of mosquitoes (Anopheles freeborni) as well as several others recovered from domestic rabbits, were of uniformly high virulence and similar in other characteristics. In a limited serologic survey, few brush rabbits and no cottontails (S. audubonii) had complement-fixing antibodies to myxomatosis. However, it was found that detectable antibodies decay rapidly in the brush rabbit. Results suggest that myxomatosis was enzootic in California wild rabbits long before the first recorded outbreaks of the disease in domestic rabbits. (See also CRA 1(3):#477 and #478, 1963.)

- 63-539 A CONTRIBUTION TO THE QUESTION OF HEREDITY OF MALIGNANT MELANOMAS. (E.) Salamon, T. (Derm. Clin., U. Zurich, Switzerland), U. W. Schnyder and H. Storck. Dermatologica (Basel) 126(2):65-75, 1963.

The authors report 4 families showing possible familial melanoma: in 1 family, malignant melanoma were diagnosed in the father and daughter, while the latter's paternal aunt showed melanotic precancerosis and her nephew had a bicolored iris and numerous pigmented nevi. In a second family, malignant melanomas appeared in a mother and son, while in a third, they appeared in a girl and her maternal grandfather. In the 4th family, malignant melanomas were found in a girl and her paternal aunt, and the mother and father of the girl both had carcinomas. The authors suggest that genetic factors may play a role in the etiology of malignant melanoma, especially since pts. with melanoma almost always have freckles and blue eyes, but these do not represent the sole etiological basis. Systematic pedigree analysis and twin studies are urged.

- 63-540 MOLDY PEANUTS AND LIVER CANCERS. (E.) J.A.M.A. 184(1):57, 1963.

Aflatoxin, a toxin produced by Aspergillus flavus during storage of moldy peanuts or grain under warm, humid conditions, is extremely toxic to experimental and farm animals, with hepatic lesions predominating. Moldy corn is an important ingredient of the native African diet, and it is suggested as an etiologic factor to explain the unusually high incidence (per 100,000) of hepatic carcinoma in the Bantu (14 compared to 3.2 for U.S. Negroes and 1.7 for U.S. Caucasians).

3-541 MORBIDITY AND MORTALITY FROM LUNG CANCER IN SINGAPORE. (E.) Muir, C. S. (Dept. Path., U. Singapore). Singapore Med. J. (4):169-173, 1962.

In Singapore, in the absence of a cancer registration scheme, the number of cancer pts. admitted to a hospital has been taken to reflect morbidity. In 1957-58, 11.2% of the 3,272 cases of cancer were lung cancer; in 1957-59, lung cancer mortality accounted for 13.8% of the over-all cancer mortality in males and 6.7% in females; as elsewhere, the incidence of lung cancer was found to increase with age, reaching a maximum in the 65-75 yr. age group. Comparison of the rates for Singapore with those from other countries showed that lung cancer in men is less common in Singapore than in the U.S., England and Wales, but more common than in Scotland and Japan, while lung cancer in women is unusually prevalent in Singapore, being more common than in Australia and Japan. Possible sources of error in these statistics, however, are pointed out. Among the etiological factors which may play a role in lung cancer, the author lists smoking, air pollution and chronic inflammation (e.g. bronchitis or tuberculosis).

-542 DIAGNOSTIC ASPECTS OF CANCER OF THE UTERUS IN IRELAND. (E.) Comerford, B. (Nat'l. Maternity Hosp., Dublin, Ireland). Irish Med. Assn. 52:113-116, 1963.

A paper devoted mainly to diagnostic techniques and the importance of early diagnosis of cervical carcinoma, the author points out the pre-invasive cancer of the uterine cervix in Ireland has a probable prevalence of 578/100,000 men over 20 yr. of age, the number being increased by about 400 women a yr. About 50% of these pts. can be expected to develop invasive carcinoma during the next 17 yr., although only out 150 cases of cervical cancer are being treated annually at present. This discrepancy is probably due to poor diagnostic facilities, since the higher birth rate in Ireland than in England would probably lead to a higher incidence of cervical cancer.

-543 THE EPIDEMIOLOGIC APPROACH TO LEUKEMIA. II. GEOGRAPHIC DISTRIBUTION IN INDIANA 1951-1960. (E.) Lingeman, C. H. (Indiana U. Sch. Med., Indianapolis). J. Indiana Med. Assn. 56(4):405-411, 1963.

Examination of the death certificates for all persons registered as dying of leukemia, lymphoma or myeloma in Indiana between 1951 and 1960, 162 cases, representing an over-all incidence of 0.12% revealed 591 children aged 16 yr. or younger. In most areas, while leukemic deaths were uniformly distributed, there were 6 conspicuous geographical clusters of acute childhood leukemia. Included was the city of

Richmond, where 7/8 cases occurred in 1958-60 (and all 8 were in the same area); 2 areas in Cass Co.; areas in Wabash and Knox Co.; and Marion Co., where the over-all incidence was only 0.08% (776 cases). In Marion Co., however, 89/776 cases were in children, and 4/89 occurred in a small area in 1953-59; although the over-all incidence in Negroes was about the same as their relative population (12% of the cases), only 5.5% of the children were Negroes, under 16, and myelomas accounted for 19% of the deaths in Negroes compared to 7% for others. The geographic and temporal localizations of acute childhood leukemia are interpreted as evidence for a viral etiology of this disease, with direct or indirect transmission from pt. to pt. The author suggests that leukemia may be an unusual reaction of the body to infection with an ordinarily innocuous and ubiquitous agent (such as adenovirus type 12), as in the case of poliomyelitis, and that other extrinsic factors may play a role in triggering the neoplastic response.

63-544 MALIGNANT DEGENERATION OF CERVICAL POLYPS. (Sp.) Nogales, F. (Dept. Obstet. Gynec., U. Madrid) and J. I. Mangano. Tokoginec. Pract. 21(205):30-35, 1963.

Malignant degeneration was observed in 18/700 pts. with cervical polyps. Of these, 8 were in pts. with a healthy cervix, although in 1 the tumor extended into the cervix; 4 more cases were carcinomas of the cervix growing in a polyp-like fashion. In the remaining pts., there were 6 carcinomas of the cervix invading preexisting polyps. In the group of 8 with apparently primary degeneration of a polyp, 2 pts. were over 60 yr., 5 were 40-51 yr. and 1 was 20 yr. old.

63-545 THE PROBLEM OF CANCERIZATION OF ULCERATIVE COLITIS. REPORT OF TWO CASES. (Fr.) Girard, M., P. Bertrand, M. Pouyet, A. Bel and D. Draoui-Mahfoud. J. Med. Lyon (1029):447-462, 1963.

A 30-year-old woman with ulcerative colitis of 9 mo. duration was operated on for an acute abdominal syndrome, and was found to have a carcinoma of the sigmoid. Postoperative rectoscopy showed a normal rectal mucosa, but there was complete obstruction of the sigmoid on barium examination. A second operation, revealed a papillary carcinoma with considerable mucoid degeneration, extensive ulcerating lesions of the transverse colon with mononuclear infiltration and marked vasodilatation. The pt's. father had died of a carcinoma of the colon. A 57-year-old man with a history of intermittent diarrhea with duration over 20 yr. with recent episodes of jaundice, and an acute episode of staphylococcal enterocolitis was operated on for a large mass in the sigmoid. Macro- and microscopic examination of the operative specimen revealed a large colloidal carcinoma of the sigmoid, typical ulcerative

colitis of the upper rectum and transverse colon, and a degenerating polyp of the upper rectum. In discussion of this association, 21 other series are reviewed.

- 63-546 BRONCHIOGENIC CARCINOMA. CHANGING CONCEPTS. (E.) Blake, H. A. (Brooke Gen. Hosp., Fort Sam Houston, Texas). *Milit. Med.* 128(3):231-237, 1963.

Two serial X-rays are presented showing long standing cysts in the left upper lobe of the lung and, at a later date, squamous-cell carcinoma at the base of the long standing cysts. Seven such cases were seen by the author. Studies of lung carcinogenesis are reviewed briefly (50 references), as are diagnosis and treatment.

- 63-547 CANCER IN NORTH WALES. (E.) Beasley, W. H. (Dept. Path., Gen. Hosp., Aberystwyth, Cardiff, Wales). *Brit. Med. J.* 1:542, 1963.

In a brief reply to a letter by C. D. Legon, in which it was suggested that the Welsh have a genetic predisposition to gastric cancer on the basis of the incidence of Welsh surnames among 74 pts. with gastric cancer compared to that in the general population in Newport, Monmouthshire, the author points out that statistical analysis of Legon's own data (30.29% Welsh surnames among the pts. and 24.33% among the general population) shows no significant difference between the 2 groups.

- 63-548 ON THE DEATH RATES FROM CANCER OF THE STOMACH AND RESPIRATORY DISEASES IN 1949-53 AMONG COAL MINERS AND OTHER MALE RESIDENTS IN COUNTIES OF ENGLAND AND WALES. (E.) Stocks, P. (Dept. Biochem. Soil Sci., U. Coll. N. Wales Sch. Agr., Bangor). *Brit. J. Cancer* 16(4):592-598, 1962.

Taking standard death rates for all males aged 20-64 as 100, miners' rates for 1949-1953 exceeded these by 15% or more for the following 6 diseases: pneumoconiosis, 1,277; stomach cancer, 149; bronchitis, 135; chronic endocarditis (not rheumatic), 146; myocardial degeneration (not coronary or rheumatic), 127; respiratory tuberculosis, 119. As an example, in Glamorgan-shire, stomach cancer death rates (age-adjusted, per million) for miners was 589, for non-miners, 326, during the same period. In Glamorgan county, equivalent mean annual death rates for the same yr. and ages were: for bronchitis, miners 992, non-miners 562; respiratory tuberculosis (with and without mention of occupational pneumoconiosis), miners 905, non-miners 713. This high mortality rate was not uniformly distributed, being higher in regions of bituminous than in anthracite coal areas. In

North Wales, where stomach cancer incidence was especially high, farmers and quarrymen, as well as miners, showed mortality rates well above the national rate of 268/million. In 9 coalfield counties the excess weighted death rate ranged from +75 to +226, but whether the kind of coal or the kind of soil is responsible for the regional difference in the occupational hazard is not known. An excess of about 50% in stomach cancer among miners' wives may possibly be attributable to coal dust in their houses.

- 63-549 THE EPIDEMIOLOGY OF SKIN CANCER IN QUEENSLAND: A METHODOLOGICAL NOTE. (E.) Lancaster, H. O. (Dept. Math. Stat., U. Sydney). *Brit. J. Cancer* 16(4):811-812, 1962.

In a brief statistical criticism of an article by G. G. Carmichael (*Brit. J. Cancer* 15:425, 1961) on the epidemiology of skin cancer, in which the latter concluded that basal and squamous-cell carcinoma occur in the absence of hyperkeratosis and that solar keratosis is not a significant premalignant lesion but occurs independently, the present author disputes Carmichael's classification of the population into 8 classes; since the number of people with neither basal cell cancer, squamous-cell cancer nor solar keratosis is unknown (these persons not being hospitalized), and is apparently assumed by Carmichael to be 0. He further shows that Carmichael's data for males indicates an association between the 2 kinds of carcinoma in pts. with keratosis and between keratosis and each type of cancer in pts. with the other type. In reply, however, Carmichael points out that these associations are weaker when females are considered (which refutes the idea that keratosis is a serious premalignant condition) and that pts. with all 3 types of lesions form a small minority, while 71.7-77.1% of the cases had only 1 type. Moreover, the statistics were only meant to apply to a hospital population and cannot be extrapolated to the population at large.

- 63-550 INCIDENCE OF BENIGN NEOPLASMS, AND PRECANCEROUS AND CANCEROUS CONDITIONS IN THE RESPIRATORY PASSAGES OF FOUNDRY WORKERS, LABORING IN AN ATMOSPHERE WITH A HIGH CONTENT OF 3,4-BENZOPYRENE. (Cz.) Kolomaznik, L. (ORL Hosp. Div., Kyjov, Czech.), J. Zdražil and F. Pícha. *Cesk. Otolaryng.* 12(1):1-11, 1963.

3,4-Benzopyrene content (from spectrographic analyses) in studies of 2 foundries revealed that sedimented dust contained 0.100-14.050 mg/kg floor sweepings 0.005-0.455 mg/kg, floor sweepings containing coal tar 4.800-28.600 mg/kg, and air (unsedimented dust, smoke) contained 1.2 µg/m³. Among 70 workers at foundry A, 216 workers at foundry B, and 126 controls (employees from the engineering department), resp., av. age (yr.) was 40.1, 36, 33.5; av. exposure (yr.) was 8.5, 10 and 6. The ratio of smokers/nonsmokers was 63%:37%; 56%:44%; 51%:49%. Among smokers, av.

duration of habit (yr.) was: 13, 17, 14.2; and av. number of cigarettes smoked (probably per day) was 18.4, 17.4, 18.1. Among the foundry workers there was uncovered 1 with malignant pulmonary tumor and 9 with laryngeal neoplasms. In the latter group, 1 was a nonsmoker, exposed for 9 yr.; 5 precancerous conditions were also found. Among the foundry workers, 8 pachydermas of the larynx, 10 leukoplakias and some other precancerous conditions were found. The authors feel there is a justified suspicion that these conditions may be influenced by 3,4-benzpyrene.

3-551 TRANSFORMATION OF SENILE KERATOSIS WITH DYSKERATOSIS OF THE TYPE IN DARIER'S DISEASE INTO A DYSKERATOTIC SPINOCELLULAR CARCINOMA IN A SINGLE CASE. (Ger.) Horzelski, T. (Dermat. Clin., U. Warsaw). *Chirurgia* 14(1):37-38, 1963.

Excision of a senile keratosis persisting for 1 yr. on the cheek of a 72-year-old woman revealed the presence of dyskeratosis, acantholysis, and cavitation. Failure to heal for the next 2 yr. was followed by enlargement of the lesion, and a histological examination 3 yr. after excision revealed a spinocellular carcinoma with pronounced dyskeratosis and gland-like cavitation. At the same time, a senile keratosis persisting for 2 yr. on the forehead was histologically found to be another dyskeratosis of the Darier's type. The relationship between these lesions and adenocanthoma is discussed.

3-552 ORAL CARCINOMA: ANALYSIS OF ONE HUNDRED AND EIGHTY-NINE CASES. (E.) Gardner, J. F. (Dept. Path., Baltimore Coll. Dent. Surg., Maryland), S. Hamburger and S. Love. *J. Am. Dent. Assn.* 66(4):456-465, 1963.

A survey of the incidence, history and clinical and histological features in 189 pts. (184 males and 5 females) with intraoral carcinoma (tongue, buccal floor, lips, tonsillar region, buccal mucosa, etc. in that order) treated by the USPHS in Baltimore between 1941 and 1960 showed that oral cancer is primarily a disease of the aging white male, the group having mean age of 56.5 yr. and including only 15 non-Caucasians; 91% of the lesions were squamous cell carcinoma. Most of the pts. had been seamen, 94.2% used tobacco and/or alcohol (49.7% were heavy smokers), 43.4% were edentulous, 36% wore dental prostheses and more than 50 pts. showed poor oral hygiene. The case histories revealed a possible association between oral cancer and syphilis, diabetes mellitus, senile epithelial changes, tuberculosis, nutritional deficiencies and cardiovascular disease. Local irritation seems to be an important factor in the etiology, and an inherited predisposition is suggested.

3-553 THE SIGNIFICANCE OF TRAUMA AND INFECTION ON THE DEVELOPMENT OF TUMORS OF THE

BRAIN AND SPINAL CORD. (Rus.) Grinberg, S. A. (Kazan Sta. Inst. Orthopaed. Traumat., USSR). *Kazan Med. Zh.* 4:78-79, 1962.

Observations on pts. with tumors of the brain and spinal cord revealed that 21/80 with brain tumors had a history of previous trauma, and 16/50 with spinal cord tumors had a history of previous infections. Two case histories on trauma and infection, resp., are presented in detail. The author feels that they are not a direct cause but do play a role in the course and development of these tumors.

63-554 CONGENITAL LEUKEMIA WITHIN A FAMILY WITH TWO CASES OF STOMACH CANCER AND PARENTAL CONSANGUINITY. (E.) Shibuya, T. (Dept. Pediat., Fac. Med., Tohoku U., Sendai, Japan), K. Yoshioka, M. Sato, A. Ishigaki and Ng. Tat-Keung. *Tohoku J. Exp. Med.* 78(3):254-257, 1962.

A 40-day-old boy with myeloid leukemia was the 7th sibling in a family in which 1 boy died at 7 days of jaundice, and 1 boy and 1 girl died at 3 and 4 days, resp., of melena. A fourth male sibling was stillborn. The grandfathers of both paternal and maternal sides died of stomach cancer, and the boy's parents were first cousins.

63-555 CANCERS OF THE RIGHT COLON COMPARABLE IN ALL ASPECTS, APPEARING AND EVOLVING SIMULTANEOUSLY IN TWIN SISTERS. (Fr.) Sérafino, X. (Cancer Inst., Dakar, Senegal), P. Corrêa, I. Pouye and E. Goudote. *Bull. Soc. Med. Afr. Noire Lang. Franc.* 7(4):513-519, 1962.

Two apparently identical mulatto twin sisters aged 55 yr. were seen within a 2-week interval for abdominal tumors of about 1 yr. duration. At surgery both had carcinomas of the right colon. The authors comment on the similarity of clinical, radiological and anatomo-pathological findings in these twins.

63-556 HISTOLOGIC STUDY OF THE RELATIONSHIPS BETWEEN GASTRIC ULCERATIONS AND GASTRIC CARCINOMA. CARCINOMA IN THE INITIAL STAGES, AT THE PERIPHERY OF THE ULCER. (Fr.) Tschantz, P. (Inst. Path. Anat., U. Geneva). *Gastroenterologia (Basel)* 99(2):81-104, 1963.

Associated carcinomas were found in 43/634 (approximately 7%) sections from chronic gastric ulcers, studied after gastric resection. In 12 cases, the neoplastic invasion was too great to permit positive demonstration of the ulceration. Among the remaining 31 cases, 7 were intramucosal carcinomas; 4 were invasions of the submucosa; and 20 were invasions of the musculature. The author theorizes that atypical intramucosal glandular formations, representing regenerative epithelial changes, are potentially capable of

becoming malignant; although they recognize that gastric carcinoma may also arise from normal mucosa, without such transition. Due to the extent of invasion, it was not possible to determine which of the conditions was secondary to the other; or whether both had developed concurrently and essentially independently.

63-557 PROPERTIES AND SPREADING OF MALIGNANT TUMORS IN SOUTH KAZAKHSTAN REGION. (Rus.) Shestial'tynov, F. Ia. (South Kaz. State Oncological Dispensary Kaz. SSR). Tr. Inst. Klin. i Eksp. Khir. Akad. Nauk Kaz. SSR. 8:12-14, 1962.

In the South Kazakhstan regional cancer clinic, 1,975 pts. (1,016 city, 969 rural) in a period of 5 yr., were registered. Cancer of lower lip was found in 164 pts. (145 males, 19 females, mostly older than 30 yr.) comprising 123 Russian, 14 Kazakhs and 27 were of other nationalities; 35% were agricultural workers. Stomach cancer was found in 391 pts. (272 males, 119 females, age 20-70 yr.); in 218 pts. the cardia was affected and there was little difference in incidence between city and rural pts. Esophageal cancer was found in 258 pts. (169 males, 89 females; age was greater than 40 yr.). Among these pts., 186 were Kazakhs (the author thinks that the high incidence might be related to the consumption of hot dough). Cancer of the female genitalia was found in 314 pts. (30-69 yr.) of whom 214 were Russian, 62 Kazakhs and 38 other nationalities; 38.5% occurred in rural women. Skin cancer was found in 430 pts. (22.37% of all malignant tumors; 159 males, 271 females); frequency among the original population was 10.1%, rural 21.62%; breast cancer was found in 83 pts. (82 females, 1 male, 30-69 yr.) of whom 47 were Russian, 20 Kazakhs and 16 other nationalities. Lung cancer was found in 116 pts. (85 males, 31 females) with the same incidence in city and rural populations. In the Kazakh Republic cancer morbidity was: 30 in 1956; 34 in 1957; 46 in 1958; 53 in 1959 and 69 in 1960.

63-558 EXPERIENCE WITH THE APPEARANCE OF MALIGNANT NEOPLASMS. (Rus.) Sundetov, A. Zh. (Inst. Clin. Exp. Surg., Acad. Sci. Kazak SSR) and M. Abakov. Tr. Inst. Klin. i Eksp. Khir., Akad. Nauk Kaz. SSR 8:19-20, 1962.

Among all registered cancer pts. in the Gur'ev region from 1951-1960, the highest number showed cancer of the esophagus (46.2% in 1951, 38.7% in 1952, 48.3% in 1953, 46.4% in 1954, 57.8% in 1955, 48.5% in 1956). In the same region in 1959, 48.8% of all pts who died of cancer had cancer of the esophagus. In 1956 in the Gur'ev and Kazakhstan regions, 51% and 16.3%, resp., of all cancer deaths were due to cancer of the

esophagus, representing rates (per 100,000) of 100 and 8.5, resp. It is possible that among the pts. with diagnosis of "cancer of esophagus" were some benign tumors, mostly leiomyoma; despite this the incidence of this type of cancer in the Gur'ev region is significant. The second and third most common cancers were those of the uterus and stomach, resp.

63-559 ETIOLOGY AND INCIDENCE OF CANCER OF THE ESOPHAGUS IN AKTIUBINSK OBLAST. (Rus.) Grishin, E. N. (Inst. Clin. Exp. Surg., Acad. Sci. Kaz. SSR). Tr. Inst. Klin. i Eksp. Khir., Akad. Nauk Kaz. SSR 8:23-27, 1962.

Among the 628 cases (379 male and 249 female) of esophageal carcinoma recorded in the Aktiubinsk regional oncological clinic in 1954-60, 579 were Kazakhs and 49 were other nationalities (mostly Russians); with an over-all incidence of 15/10,000 (and twice that in Kazakhs), esophageal cancer represents 28.5% of all cancers in the oblast (region), the annual mortality of 90-95 cases equalling that from cancer of the stomach or uterus; the 628 cases were uniformly distributed throughout the oblast (453 being rural, 175 urban), with a maximum incidence between the ages of 50-70. The most commonly affected site was the lower third of the esophagus (362 cases), followed by the middle third (232 cases) and then the upper third (34 cases). Among the etiological factors suggested are congenital esophageal constriction, dietary factors and acquired habits such as belching after eating. Particular importance is ascribed to the consumption of large quantities of hot tea (often flavored with black pepper), and the gulping of large morsels of hot meat late at night as the main meal; the consumption of acidic yoghurt is also suggested as a possible factor, but the possible relationship of carcinogens such as 3,4-benzpyrene (which are sometimes found in the fish in certain areas) is doubted.

63-560 REGIONAL PECULIARITIES IN THE DISTRIBUTION OF CANCER OF THE ESOPHAGUS IN KAZAKHSTAN. (Rus.) Kolycheva, N. I. (Inst. Clin. Exp. Surg., Acad. Sci. Kaz. SSR). Tr. Inst. Klin. i Eksp. Khir., Akad. Nauk Kaz. SSR 8:28-34, 1962.

On the basis of mortality statistics and records from oncological clinics throughout the republic, cancer of the esophagus accounted for 16.2% of all cancers in Kazakhstan in 1959 (compared to 5.1% in the USSR as a whole and 12.8% in Kazakhstan in 1954); with an incidence which has doubled since 1954, to reach 12.5/100,000, cancer of the esophagus is the 2nd most common localization in Kazakhstan (7th in the USSR), especially in the rural areas where the ratio of Kazakhs is higher. The highest incidence is observed in the Gur'evsk, Semipalatinsk, Western Kazakhstan, Aktiubinsk, Pavlodarsk and Kzyl-

insk oblasts, most of which either adjoin the or contain large rivers, and have a largely akh population. Autopsy records from Gur'evsk ast for the years 1950-59, where esophageal cer represents 60% of all cancers, with an idence of 50 and a mortality rate of 82, wed esophageal cancer in 14 cases (8 women 6 men, 12/14 Kazakh) out of 1,280. Finally, tatistical study of 501 cases of esophageal cer collected in Gur'evsk oblast between 1954 1958 revealed 305 men and 196 women, with a imal incidence between 40 and 69 yr. of age, av. being somewhat lower in women; there were Kazakhs, 56 Russians and 4 others, and all upations were represented (99 factory workers, farmers, 37 fishermen, 34 oil workers and 37 ice workers). The disease affected the er third of the esophagus in 47 cases, the dle third in 203, the lower third in 145 and cardia in 72; 7.3% had concurrent or previous erculosis and 6% were alcoholics. Although eated mechanical trauma, burns from hot tea food, excessive use of alcohol, deficiencies iron and vitamins and chronic inflammation e all been suggested as etiological factors, author concludes that a combination of racteristics is responsible for the high idence of esophageal cancer in certain areas, luding the composition of the population h respect to age and sex, the type of diet habits of the predominant nationality, and properties of the soil.

561 LUNG CANCER IN KAZAKHSTAN. (Rus.) Babashev, B. S. (Inst. Clin. Exp. Surg., Acad. Sci. Kaz. SSR). Tr. Inst. Klin. i Eksp. Khir., Akad. Nauk Kaz. SSR 8:56-65, 1962.

parison of the recorded incidence (per 100,000) lung cancer in Kazakhstan during the years 1-59 showed that it increased in almost all ts of the republic, and reached a level of 0-10.3 in Semipalatinsk oblast and the city Alma Ata in 1959 (from 1.3-2.8 in 1951), pared to 1.2 in Dzhambul'sk. The incidence the entire republic increased from 1.4 in 1 to 5.1 in 1959, the urban population being e affected than the rural (6.6 and 3.8, resp.), males being affected more often than females 5 and 1.9, resp.); in some oblasts, however, incidence was higher among the rural ulation. An analysis of the case histories 54 pts. (51 male and 3 female, 30-60 yr. of but most between 41 and 50) showed that most been exposed to possibly carcinogenic fumes dusts at their place of work; 37/54 were urban 53/54 smoked a large amount. Possible ological factors included a history of chronic erstitial pneumonia in 24 cases, bronchitis in ases, and 3 cases in whom cancer developed ound an intrapulmonary foreign body.

562 DATA ON THE INCIDENCE OF SKIN CANCER AMONG THE POPULATION OF KAZAKHSTAN. (PRELIMINARY COMMUNICATION) (Rus.) Kramchaninov,

N. F. (Inst. Clin. Exp. Surg., Acad. Sci. Kaz. SSR). Tr. Inst. Klin. i Eksp. Khir., Akad. Nauk Kaz. SSR 8:73-79, 1962.

Data from the regional oncological clinics of Kazakhstan for 1951-60 show an incidence (per 100,000) of skin cancer ranging from 7.6 in the north to 24.7 in the southern oblasts, averaging 11.9 in 1959; and the cases seen in the south are generally more severe. As expected, the incidence is much lower in Kazakhs (2) than in Russians (17.3). Contrary to expectations, however, the incidence is higher in urban than in rural residents (13.6 and 8.1, resp.), and higher in females than in males (13.6 and 10.0, resp.); also, the incidence is generally low in farmers and others constantly exposed to the sun, being higher in those exposed occasionally, in whom adaptation has not developed. The most common type is squamous-cell carcinoma (67.4%); 86% of the lesions appeared on the face, especially the nose, and 3% on the neck; the wrist and forearm were more frequently affected than the shoulder, and at sites such as the ear and neck, males were affected 2-5 x more commonly than women, again confirming the role of solar irradiation. The minimal age at onset was lower in women than in men, in the south than in the north (54.9 and 65.1, resp.), and among urban than among rural residents. In 18.3% there was a history of known trauma, (usually less than 1 yr.), and 31% recalled benign lesions preceding the cancer at the same site; the av. latent period following known trauma or irradiation was (range 2-11 mo.): 4.2 mo. in females and 5.8 mo. in males. Most new cases appeared in January-March, the fewest in June. Finally, 8% of the pts. had recurrent cancers, especially on the nose, forehead and neck; these were looked upon as new lesions resulting from repeated solar irradiation. It thus appears that a combination of trauma or senile degeneration of the skin with direct solar irradiation, especially the perpendicular rays of the summer noonday sun, can lead to the development of primary or recurrent skin cancer in non-adapted subjects.

63-563 SKIN CANCER IN KAZAKHSTAN FROM THE POINT OF VIEW OF REGIONAL PATHOLOGY. (Rus.) Smirnov, V. A. (Inst. Clin. Exp. Surg., Acad. Sci. Kaz. SSR). Tr. Inst. Klin. i Eksp. Khir., Akad. Nauk Kaz. SSR 8:80-87, 1962.

Skin cancer was studied in Kazakhstan from 1953-1959. Among 621 pts. (213 males, 408 females), only 6 were descendants of Kazakhs who lived there 100-150 yr. or more; for convenience those who had settled in the area for less than this period are referred to as "newcomers". Morbidity (per 100,000) for "newcomers" was 28.2 and for Kazakhs, 2.9. Skin cancer in 1959 comprised 15.4% of all cancers, (18.1% city, 12.9% rural); incidence in the republic was 12.1 (15.6 city, and 9.4 rural). The increase in urban morbidity was explained by the higher concentration of "newcomers" in the city. For tr:

study of the effect of climatic factors, Kazakhstan was divided into 3 zones: North zone (NZ), Central (CZ) zone and South zone (SZ). Morbidity was higher in city than rural in NZ by 14.3%, in CZ by 39% and in SZ by 102.3%. Due to an increase and prolongation of sun irradiation in the South (1.5 x more than in the North), morbidity in city increased by more than twice (by 104.5%). Other literature was also reviewed (23 references).

63-564 CARCINOGENIC SUBSTANCES IN FOOD PRODUCTS. (Rus.) Dikun, P. P. Tr. Inst. Onkol., Akad. Med. Nauk SSR 4:139-154, 1962.

A review of previously published data on the comparative incidence of stomach cancer in different countries showed a wide range of values, with consistent ratios between countries for both sexes and all age groups; the incidence increases sharply with age in all countries, but has decreased over the yr. in most, while increasing in some. This would indicate a nutritional etiology, but the higher incidence (per 100,000) in Germany (57.6 in males, 40.8 in females in 1956-57) than in England or especially in the USA (16.2 in males, 9.5 in females in 1956-57) cannot be explained by differences in the caloric content, vitamin deficiencies, or the proportion of carbohydrates, proteins and fats in the diet. The generally high incidences of stomach cancer in Iceland, in the coastal inhabitants of Latvia and in workers engaged in the preparation of smoked fish and meat, as well as in Germany where much more smoked fish and sausage is eaten than in the USA, indicates a parallel between the incidence of stomach cancer and the ingestion of the carcinogens found in smoked foodstuffs. Studies have shown 3,4-benzpyrene (BP) contents between 1.9 and 6.7 µg/kg in a variety of types of smoked fish and sausage; about 65% of the BP has penetrated the casing in sausages and 14-35% can be recovered from the edible portions of fish. The diffusion of the carcinogen into the foodstuff increases with time, not only time of smoking but also time of subsequent storage. The amount of carcinogen absorbed generally depends on the temperature of the smoke used. All smoke generators which burn wood produce BP, and all technics of smoking generally introduce this carcinogen into the food; in fact, the new

electrostatic technics introduce significantly more than the usual "cold" method. Smokeless smoking using a fluid such as suggested by I. I. Lapshin does not produce BP, but apparently is unsatisfactory for other reasons. The author therefore recommends a decrease in the consumption of smoked foodstuffs, and also suggests a technic by which non-carcinogenic smoke could be produced by controlling the amount of O₂ during combustion and by appropriate filtration. (See also CRA 1(3):#437, 1963.)

63-565 CANCERS OF THE EXTREMITIES IN NEW GUINEANS. (E.) Saave, J. J. Papua N. Guinea Med. J. 6(1):17-21, 1962.

In an evaluation of cancer of the extremities in New Guinea, the clinical, radiological, and pathological records of 109 personal (hospital pts. and pts. seen on medical visits to villages) and 17 other cases are presented. Of 126 cases, 119 were epitheliomas, 3 were osteosarcomas, 2 were malignant melanomas and 2 were epithelial cancers of undetermined nature. A significant association between phagadenic ulcers of long standing and the development of epithelial cancers of the extremities was observed (119/126).

63-566 MULTIPLE NEVOID BASAL CELL CARCINOMA, ODONTOGENIC KERATOCYSTS AND SKELETAL ANOMALIES. A SYNDROME. (E.) Gorlin, R. J. (Div. Oral Path., U. Minn. Sch. Dent., Minneapolis), J. J. Yunis and N. Tuna. Acta Dermatovenereol. (Stockholm) 43(1):39-55, 1963.

Reported are 5 new cases of an autosomal dominant hereditary syndrome with poor penetrance and variable expressivity, consisting of multiple nevoid basal cell carcinoma, multiple jaw cysts and rib anomalies. Also appearing frequently, and possibly a part of the syndrome, are palmar dyskeratosis, milia, mild mandibular prognathism, vertebrae anomalies, frontal bossing, congenital hydrocephalus, dural calcification, scoliosis, and ocular anomalies. A tendency toward fibrosarcoma of the jaws and, in 1 family studied, toward high incidence of mammary cancer were considered possible additional manifestations. An anomaly of the #1 chromosomes (1 arm of 1 of the chromosomes being longer than that of its analog) was seen in 1 pt. and several members of her family; however, it could not be demonstrated in a 2nd family studied from this point of view.

See also abstract nos.: 356,439

MISCELLANEOUS

567 IMMUNOLOGICAL STUDIES OF LYMPHOID LEUKEMIA IN THE AKR MOUSE. (E.)

Thrie, R. K. (Dept. Biol., N. Tex. State U., tton), N. A. Ingebrigtsen, N. Savage, D. C. nkle and W. J. Farris. Canad. J. Biochem. (2):305-311, 1963.

ong 44 control AKR mice inj. with BW5147 tumor ogenate (0.3 ml, s.c.), 12 were dead after 12 ys, all were dead after 24 days. Addition of tiserum to normal tissues from guinea pigs orded no protection, and 9/9 were dead in 16 ys. Mice given guinea pig mouse leukemic ssue antiserum, however, showed a slight pro- ctive effect; 10/40 were dead at 12 days, and /40 at 24 days (2% survival). When the ukemic tissue antiserum used (0.4 ml) was rst adsorbed to remove precipitating antibody, y 4/30 mice were dead at 16 days after tumor oculation, and 27% survived 24 days. The unized mice succumbed, however, at slightly er 100 days. Attempts at active immunization h a single inj. of tumor tissue-oleic acid ulsion 84 days prior to challenge with tumor duced a 46% survival (8/15 dead 200 days after allenge). Inj. of a tumor preparation kept ozen for 6 mo., provided no immunity. The ctive immunity produced by tumor tissue plus eic acid was more effective and lasting than e passive protection. The mechanism of ctective action of fatty acids on tumor ssues is not completely understood.

568 A CYTOLOGICAL ANALYSIS OF THE S91 MOUSE MELANOMA IN TISSUE CULTURE. (E.)

oboda, A. E. (Lederle Lab., Am. Cyanamid Co., arl River, N. Y.) and M. J. Kopac. Ann. N. Y. ad. Sci. 100(Pt. 1):305-333, 1963.

ontrol cultures in Eagle's medium and calf serum a strain derived from the S91 mouse melanoma, ich was unable to produce melanin, showed olar or multipolar spindles, with occasional ltinucleated giant cells and 7-8 pyroninophilic oleoli per cell; there was apparently no lanin or tyrosinase, a negative dopa reaction lthough the nucleoli showed a positive gentaffin reaction), and the cells inhibited e autooxidation of dopa in the medium. Amino id deficiency or treatment with a variety of ents resulted in decreased cell division and creased cell volume, nuclear and nucleolar lume, and nucleolar and cytoplasmic pyronino- ilia. A false positive dopa reaction was oduced by methotrexate, 4-chlororesorcinol or cystine-free medium, which counteracted the hibition of dopa autooxidation; likewise, addi- on of dopa to the medium resulted in the pearance of intracellular melanin granules, e to phagocytosis of autooxidized dopa, but ne of the procedures were successful in inducing tual melanogenesis. The authors therefore nclude that this culture may have originated om cell types in the melanoma which were ver able to produce melanin.

63-569 AUTO-IMMUNE SELECTION OF CARCINOMA CELLS IN MAN. (E.) Goudie, R. B.

(Dept. Path., U. Glasgow, Scotland). Nature (London) 197:1029, 1963.

Reviewed is the loss of autoantigens from certain experimental and spontaneous human tumors. Loss of tissue-specific antigens from tumor cells has been demonstrated by the use of heterologous antibodies in tumors of hamster, rat, and man; e.g. some cells of human thyroid tumors lack a thyroid-specific autoantigen present in epithelial cells of normal and hyperplastic thyroids. If this kind of antigenic modification selectively favors the growth of tumors, as has been suggested, there should be an increased tendency toward tumor formation in diseases associated with autoimmuniza- tion. This is true in chronic thyroiditis, where autoantibodies against cytoplasmic particles are common in the serum of pts. with chronic thyroiditis, among whom thyroid carcinoma frequently occurs. It is also true in colonic epithelial cells in ulcerative colitis; this disease definitely precedes and markedly pre- disposes to colonic carcinoma. Pts. with Addisonian pernicious anemia have autoantibodies which react with the parietal cells of the stomach; and it is probable that gastric carci- noma develops more frequently in pts. with this disease.

63-570 RUSSELL'S BODIES IN ENDOCERVICAL POLYPS. (E.) Munsick, R. A. (Coll. Phys. Surg., Columbia U., New York) and N. A. Janovski.

Obstet. Gynec. 21(4):471-476, 1963.

Russell's bodies, fuchsinophilic structures originally found in the areas of round-cell infiltration of a variety of neoplasms, as well as in plasma cell cytoplasm in areas of chronic inflammation, were detected in 12 out of 25 consecutive cases of endocervical polyps. The histochemical staining properties of these bodies, which are described in detail, confirm previous findings that these bodies consist of neutral mucopolysaccharides. Their presence in endo- cervical polyps indicates an immune response to an unknown antigen, which may have a bacterial origin or be derived from contraceptive materials, douches or seminal fluid.

63-571 ROLE OF TRAUMA IN THE DEVELOPMENT OF MALIGNANT BONE TUMOURS. (E.) Krebs, C.

(Rad. Ctr. Jutland, U. Aarhus, Denmark) and K. Olsen. Acta Radiol. (Stockholm) 1(1):42-47, 1963.

In five cases, where malignancies originated at or near the site of previous injury (fracture, sprain), reappraisal of X-ray pictures taken at the time of injury, showed in 4 cases that, at the time of the original trauma there already was evidence of neoplastic destruction or development.

The fifth case was an example where metastasis occurred at the site of an injury (presumably an area of lesser resistance), remote from the primary lesion. A similar critical reappraisal of 2 other Danish series of cases, where 29/86 and 14/40 bone tumors had been preceded by trauma, showed that in only one case of each series was it impossible to rule out the assumption that the injury had caused the disease. Considering the growth rate of malignancies, any bone tumor found less than several mo. after an injury is most likely to have originated before the injury. Mechanical injury may rupture a tumor capsule, reduce general or local resistance, and promote metastatic spread, thus aggravating an existing neoplasm, but not initiating it.

- 63-572 INFLUENCE OF TUMOR FRACTIONS ON INCIDENCE OF SPONTANEOUS MAMMARY TUMORS IN C3H/HeJ MICE. (E.) Nutini, L. G. (Div. Exp. Med. Biochem., Inst. Divi Thomae, Cincinnati, Ohio), J. E. Prince, A. G. Duarte, R. Juhasz and E. S. Cook. *Proc. Soc. Exp. Biol. Med.* 112(2):315-319, 1963.

One to 6 inj. of alcohol-soluble, protein-free fractions from a transplantable and a spontaneous tumor had only inhibitory effects when inj. into C3H mice. There were no significant differences in mean latent period, mean survival after tumor onset, or mean total survival time. The author states that current work suggests that additional fractionation may lead to separation of enhancing fractions containing nucleoprotein in transplantable tumors.

- 63-573 RELATIONSHIPS BETWEEN BLOOD GROUPS AND DISEASES: FIBROMA AND CARCINOMA OF THE UTERUS. (It.) Carrera, F. (Varese Hosp., Italy). *Minerva Ginec.* 15(1):39-41, 1963.

The proportion (in %) of the various blood groups among 100 cases of uterine cancer (seen between 1959-1962), compared to a control group (1,000 cases) was: O- 38 and 43.5; for A- 54 and 39.7; for B- 6 and 12.2; and for AB- 2 and 4.1, resp. The percentages of RH⁺ and Rh⁻ subjects in the uterine cancer group were 90 and 10, resp., as compared to 82.4 and 7.6 in the control group. Distribution by site, for cancer of the cervix and corpus, resp., was: O- 17 and 21; A- 20 and 34; B- 1 and 6; and AB- 2 and 0. The respective percentages in the fibroma (229 cases) and control (1,000 cases) groups were: O- 42.4 vs. 43.5%; A- 46.2 vs. 39.7%; B- 7.0 vs. 12.2%; and AB- 4.4 vs. 4.1%. Of the fibroma-group, 87.5% were Rh⁺ (controls 82.4%) and 12.5% were Rh⁻ (controls 17.6%). There was a larger proportion of A-group subjects in the uterine cancer group, and correspondingly fewer O- and B-group subjects than among the normal controls. Also, there were more A-group subjects with cancer of the corpus than with cancer of the cervix. Differences between pt. and control groups were much less

marked in the case of uterine fibroma, but here, too, the proportion of A-group and Rh⁺ women was somewhat higher in the pt. group. It is concluded that A-Rh⁺ women carry a higher risk of uterine cancer than those with other combinations.

- 63-574 PAVEMENT CELL INTRAEPITHELIAL EPITHELIOM OF THE CERVIX. III. CHARACTERISTICS AND PATTERN OF DEVELOPMENT. (Fr.) Fruhling, L. (Strasbourg, France), E. Philippe and R. Renaud. *Ann. Anat. Path. (Paris)* 7(4):487-537, 1962.

Review of 13,691 cervical biopsies from 11,249 women operated on between 1954 and 1960 revealed 121 carcinomas *in situ* (median age 36-40 yr.), 14 early invasive carcinomas (median age 41-45), and 1,653 frankly invasive carcinomas (median age 51-55 yr.). The age distribution of the first group showed a sharp peak, while the latter two groups were broadly distributed. None of the first set of biopsies in this series included the junction area, suggesting that early changes may be restricted to the transitional zone. A review of the location of various benign lesions and of their age distribution suggests that pavement cell metaplasia of the transition zone, simple basal hyperactivity, parakeratosis, focal keratosis and later differentiated and undifferentiated epithelial hyperplasia may represent stages in tumor progression eventuating in carcinoma *in situ*. In the authors' opinion, carcinoma *in situ* begins only in functional females, although progression to frank carcinoma may require several yr. There is no evidence that some of these carcinomas *in situ* may not regress, although the high frequency of those evolving into invasive carcinomas dictates that all be treated surgically. Included is an extensive review of the pertinent literature.

- 63-575 RELATIONSHIPS BETWEEN TRANSPLANTATION IMMUNITY AND IMMUNOLOGICAL ENHANCEMENT. (E.) Haškova, V. (Inst. Exp. Biol., Acad. Sci. CSSR, Prague), J. Svoboda and V. Matoušek. *Folia Biol. (Praha)* 8(1):16-20, 1962.

After pretreatment of C57Bl mice with lyophilized Sarcoma I tumor tissue (5 mg x 4, at 4-day intervals, s.c.), subsequent inj. of solid Sarcoma I (50 mg) 4 or 10 days after the last dose resulted in statistically significant enhancement of tumor growth (compared to controls); when tumor was transplanted after 18 days, there was non-significant enhancement of tumor growth. Parallel groups of mice which were similarly immunized, responded to F1(C57Bl x A) skin graft by a second set reaction. These opposite effects may be due to the different properties of tumor tissue and of normal skin tissue. Tumor tissue can grow against a degree of transplantation immunity and, unlike skin grafts, is not dependent for its survival on intact vascularization.

-576 SERUM VITAMIN A STUDIES IN LEUKOPLAKIA AND CARCINOMA OF THE ORAL CAVITY. (E.)

hi, P. N. (Dept. Path. Dent., S.N. Med. Coll., ra, India), R. R. Bodkhe, S. Arora and M. C. ivastava. Indian J. Path. Bact. 5(1):10-16, 1962.

The average serum levels of vitamin A and carotene were 102.44 IU and 67.88 µg per 100 ml, resp., in 15 pts. with oral cancer, compared to 121.12 IU and 81.22 µg, resp., in 123 pts. with oral leukoplakia and 160.16 IU and 84.93 µg, resp., in 60 normal subjects. Subnormal serum vitamin A levels were found in 77/123 pts. with leukoplakia and in 387/555 pts. with carcinoma, but there was no correlation between the serum vitamin A level and the severity of either leukoplakia or cancer; in the case of carotene, the serum level was much lower in grade IV than grade II leukoplakia, but this relationship did not hold true for carcinoma. It thus seems that vitamin A deficiency is one of the important factors in the etiology of oral leukoplakia and oral cancer, probably via the induction of hyperkeratosis which predisposes to the development of cancer following exposure to additional stimuli.

-577 PROPAGATION ON THE GLASS SURFACE OF A CELL STRAIN "HFSg" DERIVED FROM HUMAN MYXOFIBROSARCOMA. (E.)

Gangal, S. G. (Dept. Biol., Indian Cancer Res. Ctr., Parel, Bombay-12), S. V. Mohile and K. J. Ranadive. Indian J. Med. Res. 51(1):10-17, 1963.

The human myxofibrosarcoma cell strain HFSg was studied during its establishment in continuous cultivation on glass. The cells underwent transformation from a typical spindle shaped cell, nearly diploid, with few mitotic abnormalities (generations 1-15), through a transitional phase containing flattened prillary cells, few mitoses, and wide variations in chromosome number (generations 16-26), to a stable epithelial line showing a membrane-like growth pattern with a predominantly near-diploid chromosome number, and a changed chromosomal morphology (generations 26-80). Fresh tumor cells and cultured cells from generations 10 and 12 failed to produce tumors after transplantation to cortisone-treated hamster cheek pouches. With the transformed epithelial-like HFSg line, however, 4/6 such inoc. (2-3 million cells in cortisone-treated hamsters) produced small fibrosarcomas within a week.

-578 TWENTY-YEAR PREDICTION ON CANCER OF THE LUNG. (E.) Cancer Bull. (Texas)

(2):26-31, 1963.

This verbatim excerpt from the findings of a prediction panel on the mortality from lung cancer during the coming 20 yr., the death rate in males is variously estimated: at 70/100,000

of population by a statistician projecting from current trends (the rising death rates during the past 10 yr.); at 45 by a pathologist on the basis of expected improvements in prevention and early detection technics; at 40 by an internist, on the grounds of a shortly anticipated leveling off of urbanization; at 50 by a surgeon, despite his failure to foresee improvements through surgery; at 65 by a radiologist, based on the rising incidence curve; at 65 by a statistician, partly because of rising cigarette consumption; at 60 by an epidemiologist on the basis of local and international studies showing the concomitant increases of cigarette consumption and lung cancer incidence. In all, the av. death rate from lung cancer in males predicted for 1980 is 57/100,000 of population. Brief discussions are included on the latency period for lung carcinogenesis in smokers, sex differences in lung cancer incidence, and the significance of surveys of physicians' smoking habits.

63-579 ATYPICAL EPITHELIAL CHANGES IN THE

UTERINE CERVIX. (E.) Kirkland, J. A. (Queen Elizabeth Hosp., Woodville, S. Australia). J. Clin. Path. 16(2):150-154, 1963.

In a re-study of surgical material originally reported as suspicious or potentially malignant from 66 pts., after follow-up of 3-12 yr., 62 were living; 46 had had no further treatment. These 62 had no invasive or in situ carcinoma, and of 36 examined cytologically only one showed a suspicious smear. The 25 pts. not personally examined were reported by their physicians to be free from any significant cervical lesion. When sections from 15 cases of probable carcinoma in situ were submitted to seven pathologists for diagnosis, 66.6% favored carcinoma in situ. Early invasion was favored in 13.3%; in 20%, the opinions were either suspicious or negative. It is concluded that atypical epithelial changes of the uterine cervix over a period of 3-12 yr. are unlikely to progress to carcinoma.

63-580 POSSIBLE ROLE OF LYMPHOID TISSUE

ANTIBODY IN IMMUNOLOGIC DEFICIENCY STATES. (E., Abstract) Nagaya, H. (Dept. Med., Duke U. Med. Ctr., Durham, N.C.) and H. O. Sieker. Clin. Res. 11(2):205, 1963.

Anti-rat-lymph-node serum (ARLS) produced in rabbits by inj. of rat lymph node homogenates and Freund's adjuvant, caused death with hemorrhage and edema of the lungs when given i.v. to rats. The same effect was observed with ARLS absorbed on rat serum, but not on lymph node homogenates. Rats receiving ARLS i.p. and sacrificed from 3-28 days showed areas of hemorrhage, necrosis and early fibrosis of the lung, enlarged lymph nodes and spleen. Leukopenia occurred within 1 hr., followed by absolute lymphopenia of 48-hr. duration. In vitro, ARLS agglutinated rat lympho-

cytes. The delayed skin reaction to bovine serum albumin in rats was significantly depressed when tested 48 hr. after i.p. ARLS. Rabbit serum containing antibody against rat serum did not suppress the delayed reaction. These studies suggest the possible role of lymphoid tissue antibody in the production of certain features of immunologic deficiency states, including sarcoidosis and Hodgkin's disease.

- 63-581 MITOTIC ACTIVITY OF HYPERPLASTIC ALVEOLAR NODULES AND OF NORMAL LOBULES IN THE MAMMARY GLANDS OF C3H/Crgl FEMALE MICE. (E.) Banerjee, M. R. (Cancer Res. Genet. Lab., U. Calif., Berkeley). *Lavori Inst. Anat. U. Perugia* 22(3):177-183, 1962.

Mitotic index (MI) of normal lobules and hyperplastic alveolar nodules from the mammary glands of C3H/Crgl female mice was determined by counting the number of epithelial cells in metaphase/number of epithelial cells enclosed within a unit area 4 hr. after admin. of colchicine (6 µg/g, i.p.). In lobules taken from 4-15-day pregnant females aged 4 mo. and from 3-15-day pregnant females aged 9-10 mo., mean MI was 0.0298 and 0.0249, resp.; there was little or no variability among 55 gland pieces examined. In a group of 35 nodules from 7 multiparous, non-pregnant, tumor-bearing females, the av. MI was 0.0086; 6/7 animals showed great variability in the MI among individual nodules. Prior studies have demonstrated the existence of variant cell types in nodule cell populations. The origin and accumulation of the stable variant in a nodule with a rapid rate of cell turnover would tend to give more cells of the new type in it than in a nodule with a low cell turnover. If a lower limit exists on the number of physiologically potent cells necessary to initiate growth in a tissue, then variability in growth rate would result following transplantation of various nodules to a new host.

- 63-582 SURGICAL OPERATIONS AND METASTATIC MANIFESTATIONS OF LATENT TUMOR CELLS. EXPERIMENTAL STUDIES. (It.) Sforza, M. (Inst. Pharmacol., U. Milan, Italy) and P. Cagliani. *Biol. Lat. (Milano)* 15(2):183-187, 1962.

The i.v. inj. of 30-50,000 Walker 256 ascites carcinosarcoma cells or 20,000 DS ascites carcinosarcoma cells into Sprague-Dawley rats did not produce any metastases in the lungs or other organs. However, after partial hepatectomy either 5 or 30 days after inj. of Walker tumor cells, pulmonary metastases were detected in 6/20 rats, as well as in 2/10 subjected to splenectomy after 30 days and 1/10 splenectomized 5 days after inj.; simple laparotomy had no effect. In the case of the DS tumor, operations 30 days after inoc. had no effect, but after partial hepatectomy, pulmonary metastases were found in 6/10 rats, in 4/10 subjected to splenectomy and 3/10 subjected to laparotomy

(all 5 days after inoc.). No metastases were found in other organs in either group. It thus seems that serious surgical stress can disturb the body equilibrium and provide conditions for the development of latent circulating tumor cells.

- 63-583 "MORPHOLOGICALLY NORMAL" HAMSTER CELLS WITH MALIGNANT PROPERTIES. (E.) Defendi, V. (Wistar Inst. Anat. Biol., Philadelphia), J. Lehman and P. Kraemer. *Virology* 19(4):592-598, 1963.

One of 4 sublines of clone C13 (C13/798) from BHK21, (obtained from a neonatal Syrian hamster kidney) was studied and found to be all of a male karyotype, with a predominant aneuploid number of 44, and to show no change in stemline up to 16 passages. However, 3 of the sublines were able to induce tumors in adult female Syrian hamsters at a low cell dosage of 8×10^1 to 1×10^4 ; the remaining subline, C13/406, required an inoculum of 0.6×10^6 . All tumors were fairly well differentiated fibrosarcomas, and appeared and grew rapidly, causing occasional lung metastases. Two of the tumors, H62-263 and H62-361 (from C13/798 cells) had male karyotypes; however, the first showed a definite shift to a stemline with 45 chromosomes, while the second resembled the donor cells. Pre-immunization of hamsters with polyoma virus did not confer resistance to the C13 tumors. Moreover, on infection of C13 culture with polyoma virus, there was a characteristic change of morphology at 5-6 weeks, including loss of cell orientation and of contact inhibition. Tumor inducing properties in hamsters remained unaltered.

- 63-584 SPONTANEOUS MALIGNANT PLASMACYTIC MANIFESTATIONS OF THE P.S. STRAIN AND THEIR APPEARANCE FOLLOWING INJECTION OF CELL FREE P.S. EXTRACTS IN P.S. MICE OR IN OTHER STRAINS. (Fr.) Mouriquand, C. (Inst. Pasteur Lyon, France) and J. Mouriquand. *C.R. Soc. Biol. (Paris)* 156(11):1865-1867, 1962.

In the P.S. mouse strain, in which spontaneous plasmacytosis is rare, 3 were observed in 10 early generations comprising 736 malignancies, and 4 in the last 8 generations, av. latent period was 6 mo. When 644 newborn P.S. mice received cell free P.S. leukemia extracts, 20.7% survived weaning; among 120 malignancies, 8 were malignant plasmacytosis and appeared on the av. at 6 mo. of age. Among 150 Swiss mice inj. with the cell free extracts, 91 survived weaning, 46 developed malignancies of which 8 were malignant plasmacytosis, appearing around 7.7 mo. In a current experiment with an unstated strain, 31/84 mice survived after inj. of the cell free extracts, and so far 8 have developed malignancies, 5 being malignant plasmacytosis. Results suggest that the evolution of malignant plasmacytosis is derived from an initial malignant lymphoid proliferation, possibly as a result of an exaggerated immunologic reaction.

585 AN ASSOCIATION OF TRANSPLANTATION ANTIGENS WITH MICROSOMAL LIPOPROTEINS NORMAL AND MALIGNANT MOUSE TISSUES. Manson, A. (Wistar Inst Anat. Biol., Philadelphia, Pa.), G. V. Foschi and J. Palm. *J. Cell. Comp. Physiol.* 61(2):109-115, 1963.

lipoprotein fractions, microsomal and non-microsomal, from DBA/2 L-5178Y ascites tumor and normal tissues were tested for homograft sensitizing antigens in C57BL/6 mice. All the detectable transplantation antigens were found in the microsomal lipoproteins of the ascites tumor, and of the spleen. A dose of 50 µg of tumor, or of 25 µg spleen material was adequate to sensitize a C57BL/6 mouse, while 1 mg/mouse of non-microsomal lipoprotein from the same source was inactive. In contrast, neither the lipoprotein fractions from DBA/2 liver nor homogenates caused an accelerated rejection of 1/2 skin homografts. The microsomal lipoproteins isolated from L-5178Y were highly specific and efficient inhibitors of DBA/2 hemagglutinins, detectable in amounts of 2-4 µg protein, whereas non-microsomal lipoproteins from the same source were inactive in 30-60 µg amounts. Microsomal lipoprotein fractions from normal tissues also caused specific inhibition *in vitro*; spleen from spleen were approximately 4x as active as those of liver. Anti-DBA/2 hemagglutinins were elicited in C3H mice by the respective microsomal lipoprotein fractions. The hypothesis is presented that the endoplasmic reticulum is a major site of the transplantation antigens detected in these tests.

586 ADMINISTRATION OF FIBRINOLYSIN ACTIVATORS AND OF ANTIFIBRINOLYSINS IN THE HEMATOGENIC DISTRIBUTION OF METASTASES IN WALKER CARCINOSARCOMA. (It.) Cagliani, P. (Inst. Pharmacol., U. Milan, Italy), V. Marino and M. Sforza. *Biol. Lat. (Milano)* 15(2):175-176, 1962.

Inj. of Walker carcinoma 256 ascites (0.3 ml, 1-800,000 cells, i.v.), a 1:9 saline homogenate of solid Walker tumor, into adult, male, Sprague-Dawley rats resulted in pulmonary metastases in 100%, but no metastases in other organs. When the amount of ascites fluid was reduced by half, pulmonary metastases appeared in 30%; this was increased to 60% by i.v. treatment with Iniprol (creatic inhibitor; 50,000 units) 30 minutes before inoc., but was unaffected by Iniprol treatment 6 hr. after inoc. The incidence of pulmonary metastasis was decreased by immediate treatment with fibrinolysin or α -chymotrypsin. The decrease in the fibrinolytic activity of the blood thus seems to favor the capture and subsequent development of circulating tumor cells in the pulmonary tissue.

587 EFFECT OF VARIOUS NUTRITIONAL CONDITIONS ON THE HEMATOGENIC DISTRIBUTION OF METASTASES. (It.) Cagliani, P. (Inst. Pharmacol.,

U. Milan, Italy) and M. Sforza. *Biol. Lat. (Milano)* 15(2):177-182, 1962.

When Walker carcinoma 256 ascites (0.2 ml, 600,000 cells, i.v.) was inj. into adult, male, Sprague-Dawley rats on a normal diet of casein, rice and olive oil, postmortem examination a maximum of 15 days later showed pulmonary metastases in 6/8 inoc. into the systemic circulation and 4/9 inoc. via the portal vein; 2 of the first group showed metastasis to other organs. The incidence of metastasis was not significantly affected by maintenance on a high protein or a vitamin deficient diet for 20 days before inoc., nor by admin. of vitamin E (50 mg every other day i.m. for 10 days before and 6 days after inoc.). When a low-protein diet was given for 20 days before inoc., however, 13/17 showed pulmonary metastases and 4/17 showed other metastases following systemic inoc.; following portal inoc. 6/18 showed pulmonary metastases and 3/18 showed liver metastases. A low-protein diet thus seems to favor development of liver metastases. Lowering the capillary permeability by the admin. of a vitamin C preparation (16.6 mg vitamin C, 21 mg benzoylcarbinol and 10 mg hesperidin every other day i.m.) reduced pulmonary metastases to 4/12.

63-588 MELANOPHORE REACTION IN CASES OF MELANOMA OF THE EYEBALL. (Pol.) Dominiczak, T. (Dept. Biol. Parasitol., Med. Acad. Gdansk, Poland). *Acta Biol. Med. (Gdansk)* 6(9):285-323, 1962.

Using hypophysectomized frogs (*Rana esculenta*), the author has performed the melanophore reaction by injection of urine or serum from pts. with melanomas in different sites. In melanomas of the eyeball, diagnosed both clinically and histologically, the urine of 29/34 pts. gave a positive melanophore reaction; in cases only diagnosed clinically, 9/12 were positive. In cases of extra-orbital melanoma, all 15 were positive. Results in other cases were positive/total no.): in pts. with colored nevi, 4/7; with various other tumors, 8/10; in pts. with nonmalignant disease of the eyes, 9/16. In 61 control cases only 2 showed positive results. In 11 pts. with melanoma of the eyeball, after enucleation of the effected eye, the results were negative. With the use of serum, the following results were obtained: out of 61 cases with melanoma of the eyeball or beyond it, only 17 showed positive results. In other diseases of the eye or other tumors, only some gave positive results; 20 controls were negative. The high percentage of positive results (82.6%) indicates the possibility of using urine as an aid in recognizing this tumor.

63-589 CHEEK POUCH OF THE SYRIAN HAMSTER AND IMMUNITY TO HETEROTRANSPLANTATION OF A MURINE LEUKAEMIA. (E.) Adams, R. A. (Children's Cancer Res. Found., Children's Hosp., Boston). *Nature (London)* 197:1021-1023, 1963.

Exposure (2 mo. prior to challenge) to sensitizing inocula of AK-4, L-1210 (DBA/2), P-1534 (DBA/2), or E9514A (C3H) mouse leukemia rendered hamsters irradiated lethally 6 hr. before challenge immune to i.v. heterotransplantation of AK-4 cells, while controls showed prompt and uniform leukemic visceral infiltration and leukemic blood pictures. The failure of such cheek-pouch-transplantable tumors as L-1210, P-1534 and E9514A to implant and disseminate when admin. centrally corroborates the concept of "immunological privilege" for the cheek pouch area. However, all AK-4 and some L-1210 cheek transplants failed to grow. Further, failure of these neoplasms to grow resulted in immunization of the host against i.v. transplants, suggesting that graft antigens are capable of leaving the cheek pouch area. The species-specific immunity derived from the sensitizing inocula persisted 1-2 mo. or longer, and even overcame the specificity-loss resulting from total body irradiation. Incidentally, the prior exposure to AK-4 cells had a slight radiation-protective effect (survival of 7/38 given lethal doses).

63-590 FOCAL CELLULAR ALTERATION IN STABLE AMNION CELLS PRODUCED BY INOCULATION WITH HUMAN LEUKEMIA BRAIN EXTRACTS. (E.) Whitaker, J. A. (U. Texas Southwestern Med. Sch., Dallas), R. Bovis, S. L. Andrews and S. E. Sulkin. *Cancer Res.* 23(4):519-522, 1963.

Cell free leukemic brain extracts, prepared by a fluorocarbon emulsification technic, 12-24 hr. after inj. into 3 strains of amnion cells (Fernandes, FL, WISH) and one strain of liver cells (Chang) resulted in the appearance within cells of a feulgen-negative, RNA-positive protein material which seemed to originate in the nucleus and which gradually increased in size until the nuclear membrane ruptured, allowing the material to enter the cytoplasm, frequently causing enlargement and distortion of the cell. The same effects were obtained with serial passages of tissue culture supernatant fluids and with cells frozen and thawed in growth media. Removal of cellular debris as well as alterations in cell media did not cause an apparent loss of this effect. No apparent quantitative differences between normal and leukemic tissues in regard to protein and RNA content were apparent; no correlation was observed between the degree of cell alteration and the amount of protein or RNA. Extracts of 3 normal human brains showed no comparable change.

63-591 EFFECT ON TUMOR HOMOGRAFTS OF TREATING HOSTS WITH ANTIPROTEOLYTIC ENZYME

COMPOUNDS. (E.) Gillette, R. W. (New York Hosp. Cornell Med. Center, N. Y.), A. Findley and H. Conway. *Proc. Soc. Exp. Biol. Med.* 112(4):964-966, 1963.

When a homogenate of mammary adenocarcinoma H2712 (strain specific for C3h/HeJ mice) was homografted into C57Bl and St. A/Jax mice which received daily (starting on day of transplantation) epsilon amino-n-caproic acid (EACA; 3 mg/g body wt., i.p.), 11/25 and 6/11, resp., developed tumors. In a similar experiment where soy bean trypsin inhibitor (SBTI, 4 mg/g body wt.) was admin. daily to C57Bl mice, 3/6 developed tumors, while no tumors developed in EACA- and SBTI-untreated controls. When St. A mice received both EACA (3 mg/g body wt.) and SBTI (4 mg/g body wt.), 15/18 developed tumors. In all cases homografts regressed after reaching a maximum size in 18-20 days. Regression was not reversed by continued inj. of EACA, SBTI or both together even though viable tumor cells were present 30-40 days after homotransplantation. It appears probable that proteolytic enzymes participate in the rejection of homografted tumors; suppression of their effect (by EACA or SBTI) attenuates the immune response, and other mechanisms eventually destroy the transplant.

63-592 A FURTHER REPORT ON THE ETIOLOGY OF MYCOSIS FUNGOIDES. (Ger.) Aplas, V. (Skin Venereal Dis. Clin., Friedrich-Alexander U., Erlangen-Nürnberg, Germany). *Arch. Klin. Exp. Derm.* 216(1):63-70, 1963.

In fresh tumor tissue derived by biopsy from patients with mycosis fungoides, it was possible to demonstrate the presence of a microorganism existing in small, but measurable, intercellular colonies, which was extremely difficult to stain. Morphologically, it resembled the mycobacteria, but was more difficult to stain. The organism could not be grown successfully in any conventional medium, and did not multiply appreciably when inoc. into guinea pigs, rabbits, white mice, hamsters, or rhesus monkeys. However, when given in relatively large amounts it tended to induce granuloma at the site of inoc. Following repeated passages on the chorio-allantoic membrane of chick embryos, an adaptation took place which sometimes permitted successful inoc. into white mice, resulting in tumors of the lung, liver, and spleen, and in tissue changes similar or identical to those seen in humans with mycosis fungoides. It was concluded that the organism is a specific tissue parasite, against which the human organism is relatively defenseless.

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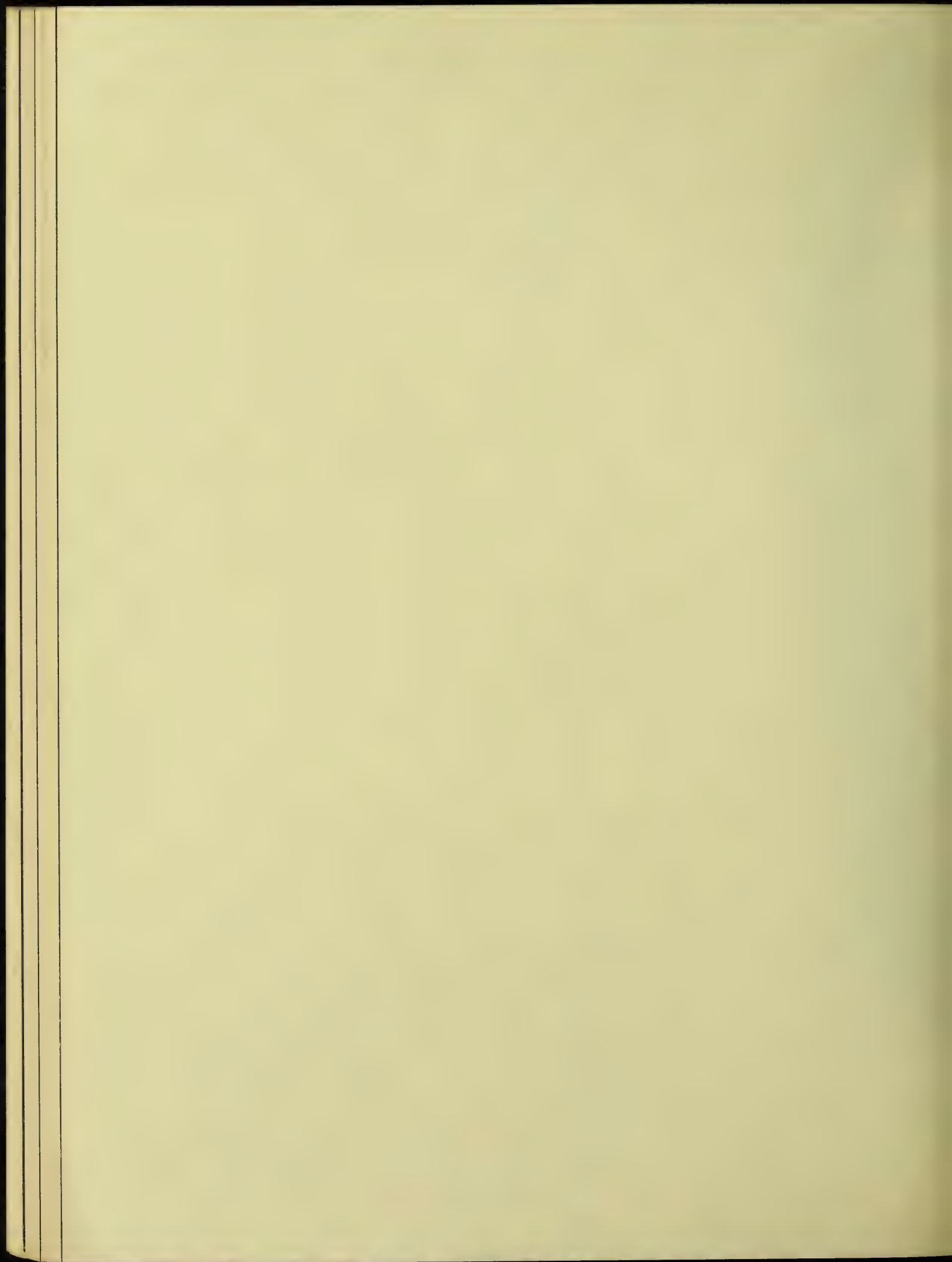
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CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service



CARCINOGENESIS ABSTRACTS

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health, USA
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FFU	focus forming unit	pt.(s)	patient(s)
g	gram(s)	RBC	reb blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
LD ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukranian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

63-593 CYTOLOGICAL AND CYTOCHEMICAL EFFECTS OF AGENTS IMPLICATED IN VARIOUS PATHOLOGICAL CONDITIONS: THE EFFECT OF VIRUSES AND OF CIGARETTE SMOKE ON THE CELL AND ITS NUCLEIC ACIDS (E.) Leuchtenberger, C. (Inst. Gen. Bot., Swiss Fed. Tech. Inst., Zurich) and R. Leuchtenberger. pp. 281-326 in International Review of Cytology. Bourne, G. H. and J. F. Danielli (Eds.). New York, Academic Press, 1963.

The biological effects of viruses and of cigarette smoke are reviewed with emphasis placed on sequential and correlated morphological and nucleic acid alterations of cells. Cell death, preceded by suppression of mitosis, decrease of nucleic acids and proteins, or cell proliferation, preceded by stimulation of mitosis associated with moderate increase of nucleic acids are considered frequent responses to agents of known and unknown nature which cause pathological conditions. Whenever cell proliferation occurs, regardless of whether this leads to regeneration or benign or malignant change, stimulation of mitosis is always associated with only moderate synthesis of intracellular nucleic acids. In a few cases where protein determinations at the cellular level have been performed, protein synthesis preceded DNA synthesis. In some instances where DNA synthesis and cell proliferation were absent (such as in surgical stress or Stage I after exposure to cigarette smoke) protein synthesis was nevertheless present. The sequence which appears nearly specific for virus infection consists of cell death, preceded by suppression of mitosis, formation of bizarre nucleic acid configurations, and striking increases in the nucleic acid content of cells. (175 references)

63-594 CARCINOGENESIS. I. MAIN THEORIES. (Fr.) Mathé, G. (Inst. Gustave-Roussy, Villejuif-Seine, France). Rev. Prat. 13(10):1067-1075, 1963.

Study of etiologic agents in carcinogenesis includes endogenous factors (primarily genetic and hormonal), considered as conditioning, rather than carcinogenic) and exogenous factors, classifiable into ionizing radiation and chemical carcinogens. A third class of agents whose nature is still unclear are viruses and nucleic acids. Studies of the mode of action of carcinogenic agents have produced two principal theories. The first would consist of an alteration of factors controlling host cell proliferation either through efficiency of factors restraining, or through excess of factors stimulating cell proliferation. The second theory is based on alterations at a cellular level through cytogenetic or, less likely, episomal (self-reproducing organelle) changes. The proposed mechanisms of carcinogenesis have included simple selection, deletion of normal cell components (primarily enzymes or enzyme systems), immunologic theories calling for new antigenic properties of specific molecules

such as lipoproteins, and finally the Warburg theory of a respiratory lesion at the level of aerobic glycolysis with compensatory increase of anaerobic metabolism. Finally the author discusses the question of multiple stages in carcinogenesis emphasizing examples of carcinogens and co-carcinogens (promoters). (8 references)

63-595 CARCINOGENESIS. II. THE ROLE OF RADIATION. (Fr.) Mathé, G. (Inst. Gustave-Roussy, Villejuif-Seine, France) and J.-L. Amiel. Rev. Prat. 13(10):1077-1084, 1963.

Included in a general review are cancers induced by radiation (local and total) of the skin, hematopoietic system, bone, lung, endocrine and other organs. The authors conclude that whatever dose-effect relationship may exist in radiation-induced neoplasia, it does not appear to be a linear one, apparently involving a complex biological mechanism which is different from that involved in other exogenous etiologic mechanisms. (2 references)

63-596 CARCINOGENESIS. III. BY CHEMICAL AGENTS. (Fr.) Mathé, G. (Inst. Gustave-Roussy, Villejuif-Seine, France) and J.-L. Amiel. Rev. Prat. 13(10):1087-1097, 1963.

Briefly reviewed are different classes of chemical carcinogens (tar derivatives, azo dyes, alkylating agents and other organic and inorganic substances); their relative carcinogenicity and factors modifying their action (including effect of substituted groups). Also discussed are anticarcinogens, cocarcinogens, the metabolism and mechanism of action of chemical and other carcinogens and prevention of carcinogenic actions in man. (5 references)

63-597 CARCINOGENESIS. IV. BY HORMONES. (Fr.) Amiel, J.-L. (Inst. Gustave-Roussy, Villejuif-Seine, France) and G. Mathé. Rev. Prat. 13(10):1099-1107, 1963.

In a general review and discussion of cancer of the endocrine glands, of the target and other organs and tissues; the authors conclude that the carcinogenic mechanisms of action of the hormonal dysfunctions involved are poorly understood at the present time. It would appear that such dysfunctions play a supportive, rather than a truly etiologic role in neoplasia, except, perhaps, in certain malignancies of the endocrine glands themselves. (8 references)

63-598 CARCINOGENESIS. V. BY VIRUSES AND NUCLEIC ACIDS. (Fr.) Mathé, G. (Inst. Gustave-Roussy, Villejuif-Seine, France). Rev. Prat. 13(10):1109-1123, 1963.

In an epidemiologic, immunologic and biochemical

review and discussion of experimental carcinogenic viruses, it is pointed out that any attempt to explain human viral carcinogenesis on the basis of experimental studies are made difficult because of species differences and even differences in individuals. Nevertheless, they feel that virology is not only one of the most promising fields of cancer research at the present time, but the one which appears to be showing the most rapid progress. (5 references)

- 63-599 CARCINOGENESIS. VI. GENETIC FACTORS. (Fr.) Amiel, J.-L. (Inst. Gustave-Roussy, Villejuif-Seine, France). Rev. Prat. 13(10):1125-1134, 1963.

In a general review and discussion, the author suggests that resistance to chemotherapeutic and other antitumoral agents may be explained in terms of the relatively high incidence of chromosomal anomalies among pts. suffering from malignancies. (1 reference)

- 63-600 ETIOLOGY AND PATHOGENESIS OF TUMORS OF THE KIDNEY. EXPERIMENTAL TUMORS. (Fr.) Pavone-Macaluso, M. (Gen. Path. Inst. Urol. Clin., U. Palermo, Italy). Gaz. Med. Franc. 70(7):1143-1189, 1963.

Various etiologic agents involved in kidney carcinogenesis and several theories of mechanisms of action are reviewed. No single factor appears to be identifiable, although renal tumors caused by viruses, estrogens, dimethylnitrosamine, lead, and irradiation are thought to deserve further investigation. Some of the 30 chemical agents listed which are effective as kidney carcinogens are: 2-acetylaminofluorene, 4-aminodiphenyl, 2-aminofluorene, β -anthraquinoline, 1,2-benzpyrene, 3,4-benzpyrene, 1,2,5,6-dibenzanthracene, diethylnitrosamine, 9,10-dimethyl-1,2-benzanthracene, 4'fluoro-4-aminodiphenyl, tar (unspecified), 20-methylcholanthrene, methanesulfonate, β -naphthylamine, radium, sulfonamides and zinc. (261 references)

- 63-601 CYTOGENETICS OF DOWN'S SYNDROME (MONGOLISM). (E.) Polani, P. E. (Guy's Hosp. Med. Sch., London). Pediat. Clin. N. Am. 10(2):423-448, 1963.

The various cytogenetic situations observed in Down's syndrome (mongolism) and produced by trisomy of chromosome #21 are discussed, including "regular" and "translocation" Down's syndrome, isochromosome formation on the long arm of #21, and chromosome mosaicism. Association between Down's syndrome and leukemia, the leukocyte changes in the former, the chromosome findings in chronic myeloid leukemia (Ph¹ chromosome) and in some familial cases of chronic lymphatic leukemia (Ch¹ chromosome) establishes an interesting relation between chromosome 21 and leukopoiesis. (130 references)

- 63-602 THE PHYSICIAN AND ENVIRONMENTAL RADIATION HAZARDS. (E.) Reiss, E. (Washington U. Med. Sch., St. Louis, Mo.) and M. L. Peterson. Pediat. Clin. N. Am. 10(2):449-468, 1963

In a general review of environmental radiation hazards, the authors conclude that the characteristics of each isotope must be considered individually, and that effective protection depends upon instituting action at a time when environmental levels are high. No satisfactory measures exist, to date, for countering the effects of fallout strontium-90; but reduction of milk intake is considered both ineffective and unjustifiable. In 1957-58, estimated thyroid irradiation from fallout ¹³¹I in children in Salt Lake City and St. Louis was estimated as 1.56 and 1.61 rad, resp., which was about 16x the background radiation of 0.1 rad. There was addition of 0.16 and 0.47 rad, resp., during 1958-59 and 0.63 and 0.32 rad, resp., in 1961-62. In April, 1963, a rainstorm brought down radioactive debris over Troy, N. Y., with ¹³¹I contamination estimated at 2-4 C/sq. mi. In Utah, in July, 1962, ¹³¹I concentration in milk was not detectable on the 6th; there was 1660 μ C on the 20th and 2050 μ C on the 25th. Countermeasures recommended during such "hot" periods are discussed at some length. (29 references)

- 63-603 SOME CURRENT PROBLEMS IN THE FIELD OF VIRUS-TUMOR RESEARCH. (Ger.) Ahlström, C. G. (Inst. Path., U. Lund, Sweden). Deutsch. Med. Wschr. 88(16):801-806, 1963.

A review and discussion of the epidemiology of virus-induced cancers (which the author considers to be virtually endemic in some species of animals), factors which inhibit and factors which activate latent viral carcinogenesis in animals (by irradiation, thymectomy, estrogens, corticosteroids, etc.); and the fact that viral carcinogenesis is not necessarily organ-specific or specific in terms of tumor type. Also discussed are the mechanisms apparently involved in viral carcinogenesis (e.g., transformation mediated by cell damage and degeneration, as well as by proliferative stimulation per se), the behavior of carcinogenic viruses in vitro, their peculiar characteristics in terms of nucleic acid content, and the possibility of a high degree of incidence of unrecognized viral carcinogenesis in man. The author concludes that the presence of virus-induced cancers in animals is a strong reason to suspect that they also exist in man; but that such existence de facto has yet to be convincingly demonstrated. (37 references)

- 63-604 THE CARCINOGENICITY AND METABOLISM OF 2-NAPHTHYLAMINE AND RELATED COMPOUNDS. (E.) Deichmann, W. B. (U. Miami Sch. Med., Coral Gables, Fla.) and J. L. Radomski. Industr. Med. Surg. 32(5):161-166, 1963.

In a review of the history of research on the mechanism of 2-naphthylamine carcinogenesis, 3 main theories are discussed: the original proposal of o-oxidation of aromatic amines to produce carcinogenic o-hydroxyamines; the 2-amino-1-naphthyl

glucuronide theory, where a carcinogenic 2-aminonaphthol would be produced by β -glucuronidase in the bladder; and the discovery of N-hydroxylation reactions leading to the hypothesis that hydroxy-compounds are the proximate carcinogens of aromatic amines. A list of other compounds known to have produced bladder cancer in dogs when administered p.o. is given, including 2-ethylaminofluorene, benzidine, 2-dimethylaminobenzene, o-aminazotoluene, 4-aminobiphenyl, and 4-nitrobiphenyl. Little is known about the metabolic fate of these compounds or of their significance in human bladder carcinogenesis. Of special interest is the observation that metabolites of tryptophan are orthohydroxyamines. (5 references)

-605 EFFECTS OF DIAGNOSTIC IRRADIATION. (E.) Lindsay, D. W. (Royal Infirmary, Edinburgh). Lancet 1:1003, 1963.

Diagnostic irradiation amounts to only 14% of background radiation--which, in turn, varies by as much as 20% in different parts of Great Britain, as much as 400% in other parts of the world, without any detectable detrimental effect in the exposed populations. It is concluded that the chances of harmful genetic effects from diagnostic radiation are too small to warrant concern. (See also CRA 1(3):#370, 1963.) (No references)

-606 A BRIEF REVIEW OF NEW METHODS OF CYTOLOGICAL RESEARCH MADE POSSIBLE BY TUMOR CELL GENETICS. (Sw.) Bergstrand, H. Scand. J. Clin. Med. 7(8):219-226, 1962.

A brief report, including a discussion of the nature of tumor progression, chromosomal aberrations and the development of new genotypes, the author suggests that chromosomal aberration and/or genetic mutation is an absolute prerequisite to the development of malignancies. The possibility that some tumors may be virus-induced is considered only consonant with this suggestion, merely implying a combination of genetically-determined predisposition with, perhaps, 1 of many possible genetic influences. The author feels that his theory goes far toward overcoming the difficulties inherent in the idea that combining the action of a tumor-inducing virus with that of a host cell can produce an autonomous cell variation without any intervening steps; however, it is only consonant with the fact that the Rous virus (for example), growing in a normal medium, can transform normal cells into malignant ones within 48 hr. (No references)

607 EXERCISE AND CANCER: A REVIEW. (E.) Rigan, D. (Waterman Gymnasium, U. Michigan, Ann Arbor). J. Am. Osteopath. Assn. 7(7):596-599, 1963.

Following a review of the somewhat limited literature on a possible relationship between exercise and resistance to cancer, the author concludes that considerable support can be given to the

hypothesis that either or both exercise and control of body wt. by diet can lead to inhibition of either spontaneous or induced cancers in laboratory animals. (20 references)

63-608 PHYSIOPATHOLOGY AND ETIOLOGY OF LEUKEMIAS. (Fr.) Bernard, J. (Res. Inst. Leukemias and Blood Dis., Saint-Louis Hosp., Paris). Rev. Franc. Etud. Clin. Biol. 8(3):281-291, 1963.

A review including a discussion of initial stages of human leukemia, chromosomal changes and viral theories. Aside from sporadic observations of hemolytic, hypoplastic, erythroblastic, or mature granulocyte changes in pts. later found to have leukemia, recent studies have emphasized two concepts: the existence of predisposing factors as well as of exterior etiologic agents, and the long lag between leukemogenic action and development of the disease. Until recent findings of chromosomal aberrations in certain forms of human leukemias, evidence of the existence of a genetic factor in humans rested on the finding of leukemia in several members of one family or in monozygotic twins, and statistically increased incidence of leukemias among mongoloids. Progress in the understanding of latent virus infection together with the finding of viral leukemias in animals have led to attempts at transmission of leukemias from tissues of diseased humans into animals. The variability of results suggest that little is known about stages at which the disease may be preferentially transmitted, and about suitable host animals. Epidemiologic studies are also in progress; some, such as that of malignant lymphoma in Africa and the epizootic in northern Europe, have been used as evidence for a viral etiology in human leukemias. (46 references)

63-609 STATISTICAL STUDIES OF THE ETIOLOGY OF BRONCHOGENIC CANCER. (Fr.) Schwartz, D. (Inst. Gustave-Roussy, Villejuif-Seine, France) and R. Flamant. Rev. Tuberc. (Paris) 26(2):5-15, 1963.

In a review of statistical studies on the etiology of bronchogenic cancer, emphasis is placed on the role of tobacco (especially cigarettes) and, as possible secondary factors, atmospheric pollution and certain occupational exposures (the handling of radioactive minerals, nickel, chromates, asbestos) and exposure within gas factories. Analogous, but still unproven roles may be played by arsenic, beryllium, isopropanol, some mineral oils, and copper. Workers exposed to diesel oil or in industries producing a high incidence of silicosis do not appear to be affected. (20 references)

63-610 EXPERIMENTAL INDUCTION OF BRONCHIAL CANCER. (Fr.) Zajdela, F. (Curie Found., Paris). Revue Tuberc. (Paris) 26(12):35-39, 1963.

Recent findings on induction of epidermoid bronchogenic carcinoma are briefly reviewed. Among experimental problems the author points out that mice are too susceptible, while rats and hamsters

are possibly resistant to experimental lung cancer induction. Variable results have been obtained in attempts to induce cancers from tars introduced directly into the bronchial tree, probably because of unsatisfactory technics. A specific problem in induction of bronchogenic cancer is the necessity to attack the basal cell of the bronchial epithelium; since the cells are protected by mucus and by the mechanism of expectoration, an effective agent may be that which is solubilized more easily and which may prevent expectoration. Chronic inflammation may also be a factor in favoring metaplasia. Finally the proven existence of areas of cicatrization after treatment with carcinogens, and, an as yet unclarified sex factor, appear to be important. (No references)

- 63-611 CARCINOMA OF THE STOMACH IN THIS COUNTRY AND IN THE ORIENT. (E.)
Walters, W. (Mayo Clin., Rochester, Minn.).
Am. Surg. 29(6):454-456, 1963.

In the USA, the death rate (per 100,000) from carcinoma of the stomach was 22 and 13 in 1930 and 1956, resp.; the 1956 death rate in Japan was 50. In Japan the diet of the Japanese may contribute to the high incidence of carcinoma of the stomach; delay in operation, may contribute to the high death rate. In the republics of the USSR bordering the Sea of Japan where the diet resembles that of the Japanese (hot rice, rice wine, raw fish and pickled vegetables with little animal protein), the cancer death rate is nearly double that of the central and western republics where a diet similar to that of Europe is eaten. The high incidence of malignant cells in gastric ulcerating lesions and the preponderance of gastric over duodenal ulcerations may be significant in the high incidence of gastric cancer among Japanese. It is speculated that an adrenal cortical steroid imbalance may develop in Japanese males over 50 yr. of age. (8 references)

- 63-612 EXPERIMENTALLY-INDUCED ERYTHROLEUKEMIA IN FOWL AS AN ILLUSTRATION OF ACUTE LEUKEMIA. (Ger.) Ambs, E. (Pediat. Clin., Julius-Maximilians-U., Würzburg, Germany) and B. Thorell. *Folia Haemat. (Frankfurt)* 8(1-4): 262-268, 1963.

In a review of previously published findings, the authors conclude that experimentally-induced erythroleukemia in fowl is of viral origin, and that the irreversible leukemic process begins with localization of the viruses in a few, primitive, bone marrow erythroblasts, from which focus they begin to spread. The appearance of leukemic cells in the peripheral blood is regarded as the final stage of a series of pathological differentiations and developmental anomalies involving metabolic abnormalities (especially as concerns the nucleotides). The

chromosomal changes, seen toward the end of this series of developmental anomalies, is not primarily involved in leukemogenesis; caution must be exercised against drawing parallels between the phenomena discussed and the development of acute leukemias in man, in view of the present lack of pertinent information. (23 references)

- 63-613 ULTRAVIOLET EFFECT ON THE SKIN AND SUNSCREEN. (Jap.) Ueta, A. (Dept. Med. Chem., Kurume U. Sch. Med., Japan) and R. Ogura. *Nisshin Igaku (Jap. J. Med. Progress)* 49(7):439-448, 1962.

In the face of the assumption that sunlight was beneficial for the skin and general health, the authors review the subject in the light of the recent findings that UV light can be carcinogenic. An analysis is made of the UV spectrum according to different effects on the skin (germicidal, erythematous). Also discussed is the pathogenesis of sunburn, sun tan and both the therapeutic (in vitiligo) and carcinogenic effects of 8-methoxypsoralen. Various sunscreen agents are discussed: the UV spectrum of some of them follow -- atabrine (maximum at 270 mμ with high absorption at 230 and 340 mμ); p-aminobenzoic acid (maximum at 266 mμ); germanin (maximum 220-310 mμ); chloroquine (maximums at 235 and 340 mμ with high absorption at 260 and 330 mμ). While sunscreen agents can prevent the photochemical degeneration caused by sunlight, and can decrease the incidence of experimentally induced UV tumors, they should be investigated not only from the standpoint of their absorption spectrum but also according to their effects on protein and nucleic acid metabolism as well as effects on enzyme systems. (See also CRA 1(4):#621, 1963.) (33 references)

- 63-614 ATMOSPHERIC FACTORS IN PATHOGENESIS OF LUNG CANCER. (E.) Kotin, P. (NCI, Bethesda, Md.) and H. L. Falk. Pp. 475-514 in *Advances in Cancer Research*, Vol. 7. Haddow, A. and S. Weinhouse (Eds.). New York, Academic Press Inc., 1963.

After examination of the authenticity of the real increase in lung cancer, and relation of incidence to urban-rural differences, epidemiological significance of airborne carcinogens (immigration studies, industrial versus ordinary insurance policy holders), factors related to sexual differences (smoking patterns in women, steroidal factors), and temporal and geographic variations in incidence (time of onset in relation to industrialization, variations within countries and epidemiological laboratory correlation), the major portion of this review is devoted to experimental considerations and bioassay studies of suspect materials. Analysis of airborne material reveals the presence of polycyclic aromatic hydrocarbons (PAH), and especially 3,4-benzpyrene; the amount of these materials in the

atmosphere is not always correlated with what has been found in smoke. The amount of PAH in urban areas is typically many times that found in rural or nonurban areas. Varying content of PAH is partly ascribed to auto and diesel exhaust (although the latter can be undetectable when operating at maximum efficiency) and the degree of use of certain materials, such as auto tires, which through wear and tear release dusts from which carcinogenic PAH may be eluted. Survival studies of both crystalline PAH and those adsorbed on soot demonstrate their persistence (even in strong oxidizing atmospheres such as Los Angeles smog) for long enough periods to be a factor in the pathogenesis of lung cancer. Certain related phenomena are reviewed, such as inhalation exposure to 3,4-benzpyrene, the role of anticarcinogens (closely related non-carcinogenic compounds) and the relation of particle size and elution to host entry. Unburned gasoline (or diesel fuel) in exhausts undergo oxidation in the presence of oxides of nitrogen in a photochemical reaction to give rise to a broad group of peroxides, including compounds with epoxidic linkages. In addition to the carcinogenic hydrocarbons, trace amounts of other known or suspect carcinogenic agents have been identified; while they are usually primarily industrial in source, one must now add the atmospheric contamination secondary to the detonation of nuclear devices. After inhalation of carcinogenic material sufficient contact must be demonstrated. In this connection the effect of a number of compounds on ciliary motion and mucous flow is reviewed. Metabolic factors are also considered; metabolites of many carcinogens are much less carcinogenic or totally ineffective contrasted with the parent hydrocarbon. There is an etiological relationship between chronic respiratory disease and lung cancer. Bioassay studies have shown that materials in the atmosphere can produce skin cancer and mesenchymal sarcomas following painting and injury in experimental animals. In the overall evaluation of the pathogenesis of lung cancer, certain epidemiological factors must always be taken into consideration: (1) the relatively high attack rate, (2) the long induction period, (3) the frequency of removal of a case from the biologically significant milieu and hence the appearance of the responsible agent or agents at the time of tumor manifestation, and (4) the remote likelihood of the combined effect of multiple factors. (193 references)

615 ULTRASTRUCTURE IN BIOLOGICAL SYSTEMS.
VOL. I. TUMORS INDUCED BY VIRUSES:
ULTRASTRUCTURAL STUDIES. (E.) Dalton, A. J.
F. Haguenau (Eds.) 29 pp.; illustr.
Academic Press, New York, 1962. \$9.50.

Detailed reviews of 7 classes of viruses and agents are given by 8 authors in this profusely illustrated first volume of a series devoted to ultrastructure in biological systems. The detailed ultrastructure given for the agents *in vitro* and *in vivo*, is given against the background of the significant progress in each field. In the review (200 references) of the avian sarcoma-leukosis complex (Rous sarcoma, myeloblastosis and erythroblastosis), F. Haguenau and J. W. Beard in summary state the past decade has seen the transition from studies yielding chiefly qualitative and relative value to the development of techniques which afford quantitative measurement of absolute meaning in the areas of biology, chemistry and biophysics. K-H. Hollmann, in the review (88 references) of infectious papillomatosis of rabbits (Shope), discusses the incidence and transmission, histology, growth, humoral factors and the physical properties and purification of the virus. The present unresolved status of the masking and the role of the virus in papilloma-derived carcinoma is outlined (88 references). In the review (115 references) of the Shope fibroma virus of rabbits, by H. Febvre, the clinical and pathological aspects of the disease are discussed along with detailed treatment of the agent, its multiplication cycle and the reactivation phenomenon between fibroma and myxoma viruses. The fact that this oncogenic virus is related to the group of pox viruses, makes it unique as a tool among tumor viruses. In the case of the milk agent, D. H. Moore reviews (84 references) the structure and origin of B particles, with comments on the nucleoid and on intracytoplasmic particles. Also treated is the agent in various tissue, tumor, and organ cultures as well as the quantitative aspects in various strains of mice, their absence in organs of tumor-bearing mice and the status of work relative to occurrence in human mammary carcinoma. R. R. Dourmashkin reviews (42 references) the ultra structure of polyoma virus in culture and *in vivo*. The various types of particles are discussed along with treatment of the confusing matter of terminology. A critical review is given of the relationship of polyoma virus to mouse leukemia and to parotid gland tumors induced by extracts of leukemic AK mice. E. de Harven reviews (36 references) the ultrastructure of the Gross and Friend mouse leukemia viruses and the related pertinent biological, immunological and chemical data. In the concluding section, A. J. Dalton reviews (15 references) electron microscope observations on the Moloney agent; included is a comparison of the Moloney leukemia with the Gross and Friend leukemias. Besides the subject index, there is an index of all authors referred to in the various presentations.

See also abstract no. 654

PHYSICAL CARCINOGENESIS

- 63-616 CONTRIBUTION TO THE STUDY OF X-RAY-INDUCED SARCOMA. (A CASE OF SARCOMA ARISING FROM AND X-IRRADIATED LUPUS, IN MAN. X-RAY-INDUCED SARCOMA IN THE GUINEA PIG.) (Ger.) Maggiora, A. (Dermat. Clin., U. Geneva), E. Bujard and W. Jadassohn. *Derm. Wschr.* 147(9): 209-215, 1963.

A pt. with lupus vulgaris of 24 yr. standing received 11 X-ray treatments over the course of approximately 8 mos.; followed, 4 yr. later, by 2 X-irradiations and local radium because of a tentative biopsy diagnosis of carcinoma. Twenty yr. later, the condition was diagnosed as typical lupus vulgaris. Ten yr. later (i.e., 59 yr. after the first lesions were noted), a histologically confirmed polymorphocellular sarcoma had developed. Tumor regression was virtually complete after 4050 r X-ray over 32 days; but 10 wk. later, a recurrence appeared and was refractory to further, daily X-irradiation. At autopsy, later, sarcomatous metastases were demonstrated in the regional lymph nodes and the lungs.

- 63-617 EXPERIMENTAL CELLOPHANE RHABDOMYOBLASTOMA TsRM-1 AND ITS BIOLOGICAL PROPERTIES. (Rus.) Studitskii, A. N. (A. N. Svertsov Inst. Anim. Morphol., Acad. Sci. USSR, Moscow). *Dokl. Akad. Nauk SSSR* 146(3):724-727, 1962.

Musculus gastrocnemius (MG) of the right extremity of 10 white rats (120-150 g) was wrapped in cellophane, and 12 mo. later 2 animals were sacrificed. Microscopically, around the cellophane membrane, dense cicatricial tissue was observed without any changes in the muscle except a slight hyperplasia of the endomysium in the region adjacent to that tissue. First tumors developed after 14 and 15 mo.; 2 mo. later both reached the size of a chicken egg. Ground tumor tissue transplant (s.c.) into the upper part of the hip or at the site where the muscle was removed showed slow growth. After 8 mo. the growths were still discrete; one-half of the transplants were resorbed after 2-3 mo. Rapid growth was found only in 2 cases: both tumors after 8 mo. were about the size of a chicken egg, and were closely adherent to the muscle. After the 1st passage, transplant growth was slow; beginning with the 3rd passage growth rate of the transplant increased reaching chicken egg size after 1 mo. In some cases transplants reached a large size in 1 wk. and exceeded the size of a chicken egg at the end of 2 wk. Often the central part of the transplant became necrotic and fistulous. Survival time of the animals with the transplanted tumors was 1-2 mo. Strain TsRM-1, (isolated from a transplant, which was grafted in the site of the removed muscle), a cellophane-induced rhabdomyoblastoma, was transplanted every 2-3 wk. for 10 mo. and according to its structure and growth characteristics was a rhabdomyoblastoma much like the tumor of origin. This characteristic structure was preserved for 15 passages

during the 10 mo. of observation. Biological characteristics of the tumor were: high growth energy, increased content of RNA (3x normal), myoblastic cells without a tendency to differentiate, characteristic giant cells, tumor tissue which contained actomycin, characteristic invasive growth into muscle, and a high degree of malignancy; in some instances there were metastases to the region of the urinary bladder.

- 63-618 DEVELOPMENT OF A RENAL CARCINOMA FOLLOWING THOROTRAST-PYELOGRAPHY. (Ger.) Krückmeyer, K. (Path. Inst., City Hosp. Berlin-Neukölln). *Urologe* 2(2):73-76, 1963.

Twenty-nine yr. after a retrograde pyelograph with an unknown amount of Thorotrast, a squamous cell carcinoma of the renal pelvis, accompanied by massive, inflammatory, infiltration and scarring of the renal parenchyma was found upon nephrectomy; moreover, a benign adenoma as well as adenocarcinomatous patches, fibrosis of the kidney, and deposits of radioactive Th-crystals throughout the entire area, but especially in the renal pelvis and in scar tissue were observed. A squamous cell carcinoma was also demonstrable in the periureteral fatty tissues; and degenerative changes (inflammation, hyperplasia, sclerosis, fibrosis, etc.) were seen in the ureter itself and in the perirenal fatty tissues. There were no distant metastases.

- 63-619 ARE THE URANIUM-BEARING LODS OF COAL AND MARL IN BLEIKEN AND BLAPBACH OF MEDICAL SIGNIFICANCE? (Ger.) Hubacher, O. (Dr. O. Hubacher Inst. Roentgen., Thun, Germany). *Schweiz. Med. Wschr.* 93(20):733-737, 1963.

Analyses made by the International Atomic Energy Agency and other supplementary investigations indicate that radiation from recently-discovered uranium-bearing coal and marl deposits in the Bleiken and Blapbach regions of Switzerland should not be a cause of concern from the point of view of possible pathogenic effects.

- 63-620 LATE EFFECTS OF FRACTIONATED X-IRRADIATION IN MICE. FAILURE TO PREVENT NON-THYMIC LYMPHOMAS BY THIGH-SHIELDING. (E.) Cole, L. J. (U. S. Naval Radiol. Defense Lab., San Francisco) and P. C. Nowell. *Radiat. Res.* 18(4):487-494, 1963.

In (C57L x A)F₁ female mice irradiated with 5 rads/wk. x 52 beginning at the age of 11 wk., the incidence of leukemia-lymphoma was 9/19; carcinoma, 1/19; sarcoma, 2/19, hepatoma, 3/19, and ovarian adenoma, 2/19; for those receiving a similar dose with 1 thigh shielded, the incidence of the same tumors was 7/13, 0/13, 0/13 and 2/13, resp.; for those receiving a single dose of 260 rads at 11 wk., incidence

3/19, 3/19, 1/19, 0/19 and 4/19, resp.; for those receiving 260 rads at 14 mo., incidence was 1/13, 1/13, 1/13, 0/13 and 0/13, resp. The majority of lymphomas were lymphosarcomas. The dose fractionation schedule increased lymphoma significantly; thigh shielding did not inhibit leukemogenesis under these conditions. This finding suggests that the mechanisms for irradiation-induced thymic and nonthymic lymphomas in mice may differ since in the former case, shielding of hematopoietic cells reduces lymphoma incidence. Renal hyperplasia and degeneration and liver regeneration occurred in 1/19, 1/19 and 1/19, resp., of unshielded fractionally irradiated mice 1/13, 1/13 and 1/13 of shielded mice. Median life span did not differ significantly among fractionally irradiated mice: that for mice receiving 260 rads at 14 mo., or at 11 wk., and for nonirradiated controls was 28 mo., 23 mo. and 29 mo., resp.

621 THE ACTION SPECTRUM OF 8-METHOXY-PSORALEN. (E.) Kooij, R. (Dept. Dermat., U. Cape Town, S. Africa), A. T. Neser and F. P. Scott. Brit. J. Derm. 75(6):245-248, 1963.

8-methoxypsoralen (MP; 1/1,000 soln. in ethyl alcohol) was painted on the skin of 2 white individuals before exposure to filtered conc. light, erythema and subsequent pigmentation elicited from all interference filters of 313 to 381 m μ after 5 min. exposure. The sunburn effect could only be obtained by simultaneous application of MP and irradiation. Sun barrier creams diminished but did not prevent this reaction. The effect was less marked in areas normally exposed to sun and much less obvious when the test was repeated over an area still showing pigmentation as the result of a previous test. MP extended the activity of the solar spectrum from 320-381.5 m μ and is considered to be potentially dangerous as it may be carcinogenic in combination with long wave UV light.

622 SQUAMOUS CELL CARCINOMA PRODUCED BY ULTRAVIOLET LIGHT IN HAIRLESS MICE. (E.) Winkelmann, R. K. (Mayo Clin., Rochester, Minn.), P. E. Zollman and E. J. Baldes. J. Invest. Derm. 40(5):217-224, 1963.

After UV irradiation (30 min. daily x 6/wk. at a distance of 30 inches) from above to HR-hairless mice bred on C57 leaden strain, 9/20 died without developing skin tumors (4/9 developed mammary tumors), all 11/20 which survived 6 mo. or more developed skin tumors. When the UV source was below the animals (73% transmission through cage), 9/20 developed multiple tumors on the ventral surface in 6-7 mo., 4/20 had thickened skin, 3/20 died early and were found to have renal and visceral abscesses, 4/20 died of unknown causes, none developed mammary tumors. After a similar dose of UV irradiation (no irradiation below 3100 Å), 3/20 died of enteritis; 2/20 manifested tumors, 1 of which was a carcinoma; 15/20 had normal epithelium and dermis, 1/20 developed a mammary tumor. After UV irradiation (5 min. daily x 6/wk. from a sun bulb, the approx. erythema dose), 1/20 died, 15/20 developed tumors in 7 mo., 4/20 had thickened skin, and 3/20 developed mammary tumors. In all experiments tumors on ear and preorbital tissue and inflammatory UV response were absent. The active wavelength for carcinogenesis may be 280-310 m μ . UV-induced tumors were clinically and histologically different from spontaneously occurring tumors.

63-623 A COMPARISON BETWEEN THE LATE EFFECTS OF THOROTRAST AND NON-RADIOACTIVE ZIRCONIUM HYDROXIDE SOL IN MICE. (E.) Bensted, J. P. M. (Inst. Cancer Res., London). Brit. J. Cancer 17(1):62-69, 1963.

When male Schofield mice were given Thorotrast (T, 0.1 ml i.v.) or a non-radioactive zirconium hydroxide sol contrast medium, Zirconotrast (Z, 0.1 ml i.v.) the first death from bronchopneumonia occurred in the Z group at 8 mo. Survivors, 18 mo. after treatment were: 37%, T-treated group; 22%, Z-treated group (controls, 50%). In the T-treated group, the incidence of leukemia was 3/13; pulmonary adenoma, 7/13; and hepatoma, 5/13. In the Z-treated group for the same 3 malignancies results were: 4/17; 4/17; and 5/17, resp. (controls, 3/14; 10/14; and 5/14, resp.). While one hemangio-endothelioma was seen in the T-group, a possibly similar tumor in the Z-group might indicate that the radioactivity of T may not necessarily be responsible for its apparent carcinogenic effect.

See also abstract nos.: 595,602,605,606,613,669,675,697,757

CHEMICAL CARCINOGENESIS

- 63-624 EXPERIMENTAL INDUCTION OF PULMONARY TUMORS IN MICE. (E.) Mori, K. (Showa Med. Sch., Tokyo). Showa Igakkai Zasshi (J. Showa Med. Assn.) 22(3):51-52, 1962.

Admin. of 4-nitroquinoline-N-oxide (0.25 mg/wk. x 10 s.c.) to 20 female dd mice produced multiple pulmonary adenomas (35-108 tumors/mouse) in all 10 mice which survived 224 days or more. In addition, 2 showed large invasive tumors with a polymorphic, hyperchromatic histological structure resembling either squamous cell, adenocarcinoma or columnar papillary carcinoma; serial sections of the adenomas from 5 of the remaining 8 mice also showed carcinomatous regions, indicating a gradual transformation of adenoma into carcinoma.

- 63-625 INCREASED INCIDENCE OF MELANOTIC TUMORS IN TWO STRAINS OF DROSOPHILA MELANOGASTER FOLLOWING TREATMENT WITH SODIUM FLUORIDE. (E.) Herskowitz, I. H. (Dept. Biol., St. Louis U., Missouri) and I. L. Norton. Genetics 48(2):307-310, 1963.

Both the wild Oregon R strain of Drosophila melanogaster, which very rarely develops melanotic tumors, and the tu^{50j} strain, which has a relatively strong genetic predisposition to melanotic tumor formation, showed considerable increases in the number of adults with melanotic tumors when the larvae were fed on medium containing small amounts of NaF (10-30 x 10⁻⁴ M). The induced tumor rate was always greater for the tumor-susceptible tu^{50j} strain than for Oregon R: at a dosage of 20 x 10⁻⁴ M of NaF fed to 1000 Oregon R larvae, 68.5% reached adulthood, and of these, 167 were tumorous (24.4%); of 1000 tu^{50j} larvae similarly treated, 61.5% attained adulthood, with 421 tumorous individuals (68.5%). The wild strain was therefore less sensitive to the tumorigenic effect of the administered NaF than the genetically predisposed tu^{50j} strain.

- 63-626 SEMIQUANTITATIVE EVALUATION OF THE SPOTS OF TAR POLYCYCLIC HYDROCARBONS ON PAPER CHROMATOGRAMS BY MEASUREMENT OF THEIR HORIZONTAL DIAMETERS. (E.) Malý, E. (Inst. Indust. Hyg. Occup. Med., Bratislava, Czech.). J. Chromatogr. 7(2):422-424, 1962.

The author suggests that the amount of 3,4-benzopyrene and other coal tar derivatives applied to the paper for chromatography in methanol saturated with paraffin oil may be estimated from the diameter of the spots in mm. The construction of a calibration curve with known 3,4-benzopyrene soln. is described, and the Rf values and fluorescence of some related polycyclic hydrocarbons in the same solvent system are given.

- 63-627 CHANGES IN THE GENITAL ORGANS IN GUINEA PIGS UNDER THE INFLUENCE OF PROLONGED HYPERESTROGENEMIA. (Rus.) Todortseva, M. S. (Fac. Gyn. Histo., Saratov Med. Inst., USSR). Akush. Ginek. 38(3):45-50, 1962.

Intact female guinea pigs (150-250 g), received the following hormones: 15/120, estrone (E; 1 ml (10,000 U)/wk. s.c.); 15/120, diethylstilbestrol (DES; 0.1% soln., 1 ml/wk. s.c.); 70/120, hexestrol (sinestrol, H; 0.1% soln., 1 ml/wk. s.c.); 20/120, H, 1 ml every 2 days, s.c. After 1-2 inj. there was swelling of the external genitalia, hypertrophy and pigmentation of the nipples, and epilation; 3/120 had corneal clouding. These changes occurred 1 wk. after the first inj. and were more pronounced with H than with E. Among 100 in the first 3 groups, 86 died during 1-45 wk. In the low and high dose H groups, autopsy revealed the following liver hypertrophy, fibroperitonitis in 6/70 and 4/20, resp., and inflammatory areas in the internal genitalia and intestinal loops in 10/70 of the low dose H group. The wt. of uteri progressively increased but after 19-30 inj. decreased below normal; the ovaries increased 150-200%, but after 15-19 inj. of F, DES, and H (low dose), and after 20-25 inj. of H (high dose) began to decrease. Maximum uterine wt. was 16-17 g (normal, 1-2 g). Uterine tumors developed in 20/70, and 13/20 resp., and in 5/15 of those inj. with DES; 10/38 were fibromyomas, 40 mg-2.5 g in wt., their cornu and glands were hyperplastic, and the epithelium necrotic. Tumors of the stomach, omentum, peritoneum, and the intestines developed in 11/120.

- 63-628 THE EFFECT OF CASTRATION AND OF ADDITIONAL HORMONAL TREATMENTS ON THE INDUCTION OF CERVICAL AND VULVAL TUMOURS IN MICE. (E.) Glucksmann, A. (Strangeways Res. Lab., Cambridge, England) and C. P. Cherry. Brit. J. Cancer 16(4):634-652, 1962.

To investigate the role of hormonal status in drug-induced carcinogenesis, intact and ovariectomized female C3H and Strong A mice aged 8-12 wk. were all painted intravaginally weekly with a 1% solution of 9,10-dimethyl-1,2-benzanthracene (DMBA) in acetone; some groups of castrates received hormonal stimulation, which was begun 2 wk. prior to painting. DMBA alone, in 13/17 intact mice, induced only squamous cell carcinomas, involving usually the uterus and vagina; 8/15 castrate mice developed 5 squamous cell and 3 mixed carcinomas (38% of all cancers in this group). The mixed, definitely malignant tumors contained both keratinizing squamous and columnar mucin-producing components. Of the castrated mice given diethylstilbestrol (DS; 20 µg in 200 ml of drinking water), 13/21 (62%) developed well differentiated squamous cell carcinomas of the cervix or vagina. In progesterone treated (0.2 mg x 2/wk.) castrate mice, DMBA induced carcinoma

of the cervix or vagina in 13/16 (81%); and in 12/16 (75%) of those given progesterone in pellet form (Lutocyclin; 50 mg, then 25 mg after 2 mo. and again after another 6 wk.). Of those given Eltroxin (L-thyroxine sodium; 0.01 mg/100 ml water per day + 3 µg/wk., i.m.), DMBA induced carcinomas of the cervix or vagina in 8/13, (7 squamous and one mixed). Most mice with carcinomas also formed papillomas, but some had only papillomas. Incidence of papillomas in intact mice was 7%, but rose to 31% in castrates, with or without added hormonal treatment. The proportion of carcinomas of the cervix was greater in intact than in any treated or untreated castrate group. Mucoepidermal tumors were formed in 36% of castrate mice with or without treatment with progestational hormones, but in only 3% of intact mice or in castrate mice treated with DS or thyroxine. While tumor induction time could not be measured exactly, it was longest for intact mice and shortest for castrates treated with Lutocyclin. Carcinoma of the vulva developed in 29% of the intact mice and in 87% of the castrates. All epithelial tumors (carcinoma + papilloma) arose in 65% of the intact mice and in 100% of the castrates; in castrates treated with DS, there were 76% carcinomas, 91% had all epithelial tumors; Lutocyclin, 19% carcinomas, 50% all epithelial tumors. Additional remote tumors (mostly papillomas) arose in all groups, but breast tumors only in the C3H strain. It is concluded that castration and additional hormone treatment produce different effects on DMBA carcinogenesis in the vulva and the cervix; and that hormonal influences can determine the histological type of a developing tumor. After local application of a carcinogen to the cervix, mucoepidermal tumors appear rarely in intact females, not at all in estrogen-treated castrates or intact mice; but occur more often in untreated and progesterone-treated castrates.

-629 THE RELATION BETWEEN PSEUDOPREGNANCY AND THE CHEMICAL INDUCTION BY FOUR CARCINOGENS OF MAMMARY AND OVARIAN TUMOURS IN BALB/c MICE. (E.) Biancifiori, C. (Div. Cancer Res., U. Perugia, Italy) and F. Caschera. *Brit. J. Cancer* 16(4):722-730, 1962.

Additional findings are given on a previously reported work on induced mammary tumors (see A 1(2):#201, 1963). In a group of lobectomized BALB/c mice, treated topically with 20-methylcholanthrene (20-Me) for 12 weeks followed by excision of skin tumors, 41 survived 19-56 weeks and 2 developed mammary tumors. No ovarian tumors occurred in virgin or lobectomized mice treated topically with 20-Me. After admin. of 20-Me and 9,10-dimethyl-1,2-benzanthracene (each 2 mg/2 wk., p.o.) for 8-12 wk., virgin mice, granulosa cell ovarian tumors were induced in 6/13 and 23/36, resp.; in pseudopregnant mice, results were 1/14 and 3/34, resp. After treatment for 15 wk. with

3,4-benzpyrene and 1,2,5,6-dibenzanthracene, no ovarian tumors developed in groups of virgin and pseudopregnant mice followed from ages 15-59 wk.

63-630 THE INDUCTION OF MAMMARY CANCER IN RATS. (E.) Boyland, E. (Roy. Cancer Hosp., London) and K. L. Sydnor. *Brit. J. Cancer* 16(4):731-739, 1962.

The incidence of mammary tumors in female Chester Beatty strain rats force-fed at 2-wk. intervals with 3 doses of 9,10-dimethyl-1,2-benzanthracene (DMBA; 15 mg in 1 ml arachis oil), was (mean number of tumors/rat; number tumor-bearing rats/number treated; mean latent period in days) for rats aged 30, 40, 50, or 60 days (at start of treatment) was, resp.: 4.8 in 8/8 in 40 days; 4.0 in 9/10 in 61; 2.8 in 9/10 in 63; 1.9 in 7/10 in 66. Essentially similar treatment of Wistar rats also induced multiple mammary tumors in 4-6 wk.; however, the same treatment did not induce mammary tumors in the Marshall strain and only after long periods in rats of the August strain. In Chester Beatty female rats, addition of thymine to the diet (1% dry wt. plus 0.5% in drinking water) reduced mammary cancer incidence from 11/11 to 6/11 after treatment with 2-15 mg doses of DMBA. Rats treated similarly with 3 doses of DMBA, and given 1.5% thymine or uracil, showed a prolonged mean induction time (57 and 69 days, resp.) over their controls (43 days) and fewer tumors (3.7 vs 5.6). Strain sensitivities to DMBA-induced mammary cancer were: Wistar, 11.0 tumors/rat in 11/11 in 50 days; Sprague-Dawley, 8.3 tumors/rat in 11/12 in 51 days; Chester Beatty, 2.8 tumors/rat in 9/10 rats in 51 days; August, 2.0 tumors/rat in 9/10 rats in 90 days; Marshall, no tumors in 5 rats. Toxic effects of DMBA treatment included frequent (10-40%) leukemic infiltration of kidney, liver, spleen, occasional calcium deposits in adrenals, and depression of normal weight gain. Growth inhibition was slight in rats treated with DMBA at 30 days, or fed a stock diet, was more pronounced when treatment began at 50 days, or when rats were maintained on a 20% protein diet. In rats given 133 mg/kg in 1 dose, or 60 mg/kg in 2 doses, 12/12 and 11/11 died in 14 and 26 days, resp. After i.p. admin. of DMBA (60 mg x 2 or 50 mg x 1) no mammary cancers developed; after 20-methylcholanthrene (133 mg, in 2 doses, i.p.) no mammary cancers occurred but 9/16 rats developed sarcomas. Oral admin. of DMBA or naphthalene increased ascorbic acid excretion of rats to a greater extent in Sprague-Dawley and Chester Beatty than in Marshall strain rats.

63-631 STUDIES ON RAT LIVER CELL ANTIGENS DURING THE EARLY STAGES OF AZO DYE CARCINOGENESIS. (E.) Baldwin, R. W. (Cancer Res. Lab., U. Nottingham, England). *Brit. J. Cancer* 16(4):749-756, 1962.

Immunochemical studies of liver cell sap from

adult male Wistar rats have shown that significant changes in antigenic composition occur during the early stages of 4-dimethylaminoazobenzene (DAB) carcinogenesis. In addition to changes in the conc. of normal antigenic components, at least 1 abnormal antigen was detected in the cell sap of rats treated with DAB for 4-5 wk. This antigen does not react with normal liver antigens. However, antigenic components in DAB-treated liver cell sap cross react with antiserum prepared against synthetic DAB-bovine albumin conjugates. This antiserum contains antibody directed specifically against the DAB prosthetic group and it is therefore concluded that the abnormal antigen(s) in DAB-treated liver cell sap contain bound carcinogen, or a metabolite still retaining an azobenzene structure. Although the existence of a specific immune response being elicited to liver protein complexes induced *in vivo* by DAB is not proven, it is known that such autoimmunization, particularly if accompanied by cell sensitization, could produce lesions in a variety of tissues.

63-632 OBSERVATIONS ON THE POLAROGRAPHIC CHARACTERISTICS AND CONCENTRATIONS OF PROTEIN AND SIALIC ACID IN THE SERUM OF RATS AFTER INTRAPERITONEAL INJECTIONS OF POLYCYCLIC HYDROCARBONS. (E.) Searle, C. E. (Cancer Res. Lab., Birmingham Med. Sch., England) and D. L. Woodhouse. *Brit. J. Cancer* 16(4):794-805, 1962.

The i.p. inj. of rats with 9,10-dimethylbenzanthracene (9,10-DMBA; 25 mg/kg x 2-3 on days 0, 74 and 147) or 1,2,5,6-dibenzanthracene (25 mg/kg x 3, on days 0, 50 and 102) and 2 non-carcinogenic isomers (2',6-DMBA and 1,2,3,4-dibenzanthracene) did not produce any consistent effects on the polarographic digests and filtrate tests carried out on the serum. The rats inj. with 9,10-DMBA developed massive ascites and 2/4 had sarcomas in the peritoneum when sacrificed 30.5 weeks after the first dose. No ascites was observed in rats inj. with 2',6-DMBA or either of the dibenzanthracenes, and no tumors were found at death. Conc. of total serum protein were not markedly affected by the inj., but fell during the development of ascites in 9,10-DMBA-treated rats. Serum sialic acid levels showed a sharp temporary rise after some inj. of both carcinogenic and non-carcinogenic hydrocarbons.

63-633 EXPERIMENTAL ATTEMPTS TO DEMONSTRATE AN ACTIVE CARCINOGENIC SUBSTANCE IN THE VAGINAS OF PATIENTS WITH CANCER OF THE CERVIX UTERI, ACCOMPANIED BY A STUDY OF LATENT PERIODS. (Dan.) Bang, F. (Histopath. Lab., Copenhagen). *Ugeskr. Laeg.* 125(14):506-512, 1963.

Since local carcinogenic action is probably responsible for both tar-induced cancer in animals and cervical carcinoma in women, s.c. inj. of estradiol benzoate (dose not stated) were used to induce continuous estrus in the

experimental mice and guinea pigs, accompanied by hyperplasia of the uterine corpus and endometrium and by tissue changes in the cervical canal similar to those seen in women with cervicitis and/or leukoplakia. These changes were also produced or intensified (especially in non-castrated animals) by vaginal deposition of tumor tissue derived from pts. with incipient carcinoma of the cervix; however, there was no resulting malignancy in 16.5 mo. One guinea pig (which received no tumor cells) developed a polymorphocellular sarcoma at the site of inj.; another, which received both estradiol and tumor cells, developed a spindle cell sarcoma of the flank and a benign intrauterine fibromyoma-like tumor. In preliminary studies of latency in the development of experimental cancers, and in an attempt to find accelerating or "spreading" factors which enhance tumor development, Bagg mice received 20-methylcholanthrene (20-Me; 0.3% in benzene, 1 drop topically) onto the interscapular area 3 x/wk. for 3½ mo., plus 4 inj. of an extract of homologous 20-Me-induced tumor cells into the area of latent cancerous foci at 5-day intervals during the first 3 wk. Macroscopically demonstrable tumors appeared in 12/51 treated mice at the end of 3 wk., vs. 9/52 controls which received only 20-Me; in 29/51 (vs. 22/52) at the end of 6 wk.; and in 46/51 (vs. 34/52) at the end of 9 wk.; both groups developed 100% tumor incidence rapidly thereafter. However, no significant differences were found in a similar group when inj. of tumor extract were begun following the appearance of extensive non-cancerous tissue changes in response to 20-Me.

63-634 EFFECT OF HORMONES ON PODOPHYLLIN-INDUCED VAGINAL ATYPIAS. (E.) Kline, T. S. (Michael Reese Hosp. Med. Ctr., Chicago). *Arch. Path.* 75(4):343-349, 1963.

Vaginal smears of 39 rats receiving podophyllin (10% in mineral oil, daily topical vaginal application for 1-30 days) revealed bizarrely shaped cells with markedly increased nuclear-cytoplasmic ratios resembling those exfoliated in marked dysplasia or so-called carcinoma *in situ* of the cervix uteri. Dedifferentiation of vaginal mucosal epithelium was observed. No evidence of true tumor formation or invasion was found. Estrogens (1 mg Amniotin/wk., s.c.) and/or testosterone (5 mg Testryl/wk.) before and during podophyllin admin. did not alter podophyllin activity. Hormone or mineral oil-treated controls showed no atypical changes.

63-635 TUMORIGENIC PROPERTIES OF 2-CYANO-4-AMINOSTILBENE IN RATS. (E.) Ribelin, W. E. (Environ. Health Lab., Am. Cyanamid Co., Princeton, N. J.), C. B. Shaffer and G. J. Levinskas. *Toxic. Appl. Pharmacol.* 5(3):344-349, 1963.

Repeated admin. of 2-cyano-4-aminostilbene

(20 mg x 30, s.c.) into CNF rats resulted in increased numbers of tumors compared with controls. The experimental/control ratio for number of tumors and for animals with tumors was 2.12 and 1.71, resp., for males, and 2.27 and 1.23 for females. A striking feature in treated animals was the increase of rats with multiple tumors and, also, the large number of s.c. cysts of sebaceous origin (25%). Seven fibromas and 1 fibrosarcoma were found in 40 treated rats vs. 2 fibromas in the 40 controls (male and female). Hepatomas were found in 5/20 treated males, but were absent in the other 3 groups, although other hepatic changes were common in treated animals of both groups. This apparently specific hepatic cell response to the agent occurred in well defined foci and was characterized by intense cellular vacuolization. Intervening cells had swollen granular cytoplasm, and contracted, eccentric nuclei. Occasionally, cells in degenerating areas were enlarged and hyperplastic, suggesting a stage of initial tumor development. Treated females showed a striking increase in the number of mammary fibroadenomas (13/20 vs. 2/20 in controls); a squamous cell carcinoma was also found in the treated female group.

63-636 CONTINUOUS CULTIVATION STUDIES ON A NEW CELL STRAIN "MFSg" DERIVED FROM A MOUSE FIBROSARCOMA. (E.) Ranadive, K. J. (Dept. Appl. Biol., Indian Cancer Res. Ctr., Parel Bombay), U. V. Wagh, B. N. Mashelkar and A. N. Bhisey. Indian J. Med. Sci. 17(3):216-223, 1963.

transplantable fibrosarcoma induced in inbred Swiss mice by inj. of 6,12-dimethylbenzo-1:2-b:4:5-b'-dithionaphthene s.c. has been maintained in continuous tissue culture for over 2½ yr. This MFSg strain underwent a number of changes during *in vitro* growth. For the first 20 passages the cultures contained spindle-shaped fibroblasts. By the 25th passage the fibroblasts showed a tendency to form a loose network with empty spaces. Eventually one of the fibroblasts would occupy the empty space, become flattened, and undergo several nuclear divisions to form a multinucleated giant cell. Later this would undergo several cellular divisions to form flattened Ep-L cells. A definite phenotypic change in MFSg was noted on the 67th passage. However, while cells from the 10th passage produced 100% tumors when inj. s.c. in Swiss mice, tumor formation decreased progressively with tissue culture subpassages as follows: 20th, 3/3; 35th-45th, 3/9; 60th-80th, 0/23. Nutritional requirements also have changed.

63-637 THE MANAGEMENT OF JAW TUMOURS IN THE SOUTH AFRICAN BANTU. CARCINOMA OF THE ANTRUM. (E.) Keen, P. (Non-European Hosp., Johannesburg, S. Afr.). Clin. Radiol. 14(2):250-254, 1963.

carcinoma of the antrum among the South African

Bantu, which occurs 10 x more frequently and at least a decade earlier than in pts. of European ancestry, was linked to the heavy use of a snuff mixture (2 parts tobacco powder to 1 part plant ash mixture, usually, *Aloe marlothii*) thus containing both nicotine and a series of polycyclic hydrocarbons, including 3:4-benzpyrene. In a group of 226 pts. with respiratory malignancies (seen between 1949-54), the incidence of nasopharyngeal and laryngeal malignancies was approximately equal among Bantu and European pts.; however, the incidence (percent) of cancers of the sinus was 67 and 17, resp.; that of pulmonary cancers, 5 and 54, resp. Among the Bantu, there has been a gradual decrease in the numbers of antral carcinoma presented since 1957, with a concomitant increase in pulmonary cancers, the changes paralleling a marked decrease in snuff taking and a marked increase in cigarette smoking since 1946.

63-638 MULTIPLICITY OF CARCINOMA AND SARCOMA OF RAT LIVER. (E.) Matsuyama, M. (2nd Dept. Path., Nagoya City U. Med. Sch., Japan), H. Norikawa and A. Maekawa. Nagoya Med. J. 8(1):1-4, 1962.

A Sprague-Dawley rat received a total of 880 mg of 3'-methyl-4-dimethylaminoazobenzene in Tween 80, s.c. in 37 inj. at 1-wk. intervals. At autopsy, after a total survival time of 270 days, histologic studies of the liver showed an hepatocellular carcinoma in the left lobe and a spindle cell sarcoma in the right; the latter extended into the non-malignant middle lobe and invaded the pancreas and intestine. Among 16 other rats given similar treatment, 5 survived more than 200 days, all of whom developed fatal, single hepatomas.

63-639 CARCINOGENIC EFFECT OF DIAZOMETHANE ETHYLACETATE AND AN ESTER OF N-NITROSOSARCOSINE AS AN EXAMPLE OF THE TRANSPORT-FORM, ACTIVE-FORM PRINCIPLE. (Ger.) Druckrey, H. (Clin. Surg., Albert-Ludwigs U., Freiburg/Br., Germany), R. Preussmann, G. Blum and S. Ivankovic. Naturwissenschaften 50(3):99-100, 1963.

Diazomethane ethylacetate (LD50, 400 mg/kg, p.o. in a single dose) was admin. (in drinking water), 5 mg/kg/day to 16 rats, and 10 mg/kg/day to 4 rats. After 48 days, 14 rats were still living, all of which died subsequently of carcinomatosis of the forestomach. In 8 of these rats, an additional carcinoma at the base of the tongue was noted. Both induction time and total doses necessary for the induction of tumors followed a normal logarithmic curve. Median survival time from the initiation of treatment was 575 ± 35 days, with tumors appearing virtually synchronously with death. The purified ethyl ester of N-nitrosomethylaminoacetic acid (no acute toxicity in rats in doses up to 4 g/kg, p.o.) was admin. in drinking water, 50-100 mg/kg/day to rats (number not

stated). All animals developed carcinomas, limited exclusively to the esophagus. Induction time ranged from 158-185 days. The selective or organotropic activity of diazomethane ethylacetate was ascribed to liberation of carbonium ions in the acid milieu afforded by the forestomach; that of the second compound, to an esophageal resorptive effect also seen following i.v. inj. of various nitrosamines -- as previously reported elsewhere. These results suggested that an active "transport form" of the nitrosamines may be converted *in vivo* into a specifically organotropic "active form" by chemical reaction and/or bonding.

63-640 THE RESPONSE OF MUCUS-SECRETING EPITHELIUM AND MUCUS TO IRRITANTS. (E.)

Falk, H. L. (U. Southern Cal. Sch. Med., Los Angeles), P. Kotin and W. Rowlette. *Ann. N. Y. Acad. Sci.* 106(Art. 2):583-608, 1963.

Evidence is presented for the hypothesis that chemical and physical agents (including influenza virus) interfere with the protective effect of the mucous layer covering the respiratory epithelium by modifying the quantity of mucus secreted, the rate of mucus flow, and the physical properties of the mucus. Effect of agents on rate of mucus flow (as determined by particle transport) was studied primarily using mucus-secreting ciliated epithelium from the esophageal tract of the frog. Exposure to a solution through which smoke had been drawn resulted in responses similar to those observed with ciliated tracheobronchial epithelium, consisting of a sharp initial rise at 3 min., followed by a marked drop below basal levels at about 10 min., followed by a gradual rise to near basal levels after about 30 min. Similar qualitative responses were observed on exposure of the epithelium to artificial smog, natural smog, and ozone. Applications of tar soln. from cigarette smoke caused a response, but application of the gas phase from cigarette smoke resulted in no detectable change. Agents causing an increase in the rate of mucus flow at 16 min. were 2-methyl butene-2, benzene, methanol, n-butyraldehyde, acetaldehyde, and nicotine. The last 2 had a decelerating effect after exposure. Agents causing deceleration of mucus flow at 16 min. were formaldehyde, formic acid, acetic acid, peracetic acid and nitrogen dioxide. Butadiene and acetone had no effect at 16 min. but caused an increase and decrease in rate of flow, resp., after exposure. 2-Methyl pentane, cyclohexene oxide, and phenol had no observable effects. Cholinergic agents, cholinesterase inhibitor, and arecoline prevented the sharp drop observed after exposure to cigarette smoke solutions, but did not affect the initial rate of mucus flow. Histological alterations on exposure to irritants paralleled the changes observed in mucus flow. The possible relation of influenza virus infection and air pollution to the role of alteration of mucus in the pathogenesis of lung

cancer was investigated by exposing mucus from snails to influenza virus in the presence of various ozone concentrations. As ozone concentration increased, there was considerable reduction of the inhibitory action of mucus on the influenza virus hemagglutination reaction.

63-641 MALIGNANT RESPIRATORY TRACT NEOPLASMS RELATED TO POISON GAS EXPOSURE. (E.)

Wada, S. (Dept. Inter. Med., Hiroshima U. Sch. Med., Hiroshima), Y. Nishimoto, M. Miyanishi, S. Katsuta, M. Nishiki, A. Yamada, S. Tokuoka, H. Uemura, and M. Nagai. *Hiroshima J. Med. Sci.* 11(3): 81-91, 1962.

Among 156 Japanese workers (in a single factory) dealing with poison gas -- chiefly, mustard gas (Yperite); but also Lewisite (chlorovinylarsine), hydrocyanic acid, diphenylcyanarsine, chloracetophenone, et al. -- between 1929-1945, and who died before 1961, 22 (14%) died of respiratory tract cancer, and 15 (9.6%) died of cancer of the g.i. tract (2 esophageal, 9 gastric, 2 primary hepatic, and 2 rectal). Autopsy was done on 13/22 who died of respiratory cancers; all 13 during their work and even after retirement exhibited various respiratory complaints (cough, fever, chest pain, bloody sputum). All had been exposed to mustard gas, and 1 had also been engaged in producing Lewisite gas. The period between termination of employment and the initial diagnosis of cancer was >20 yr. in 7/13; 16-20 yr. in 5; and 10 yr., 11 mo., in 1. According to site, there were 9 bronchogenic, 3 laryngeal, and 1 pharyngeal carcinomas; 9 were squamous cell and 4 undifferentiated carcinomas. All primary lesions were limited to an area from the upper respiratory tract to the 2nd and 3rd main bronchi.

63-642 THE EFFECT OF POLYCYCLIC HYDROCARBONS ON THE THERMAL DENATURATION OF DESOXYRIBONUCLEIC ACID. (E., Abstract) Boyland, E. (Royal Cancer Hosp., London) and B. Green. *Biochem. J.* 87(1):14P-15P, 1963.

Pyrene and the corresponding carcinogenic 3,4-benzpyrene (1.4 and 0.3 μ M, resp.) caused an increase in the thermal inactivation temperature (T_m) of calf-thymus DNA (0.01% in 0.001 M disodium hydrogen phosphate) of about 6°C. 1,2-Benzanthracene had a similar effect, while anthracene and 9,10-dimethyl-1,2-benzanthracene caused an increase of about 10°C. Under these conditions the stabilizing effect of the hydrocarbons is nonspecific, but may reflect some contribution of polarization and hydrophobic bonding between hydrocarbon and bases in regions where local fluctuations occur in the double helical structure of the macromolecule.

63-643 THE REACTION OF SOME COMPOUNDS OF BIOLOGICAL INTEREST WITH NUCLEIC ACIDS. (E., Abstract) Roberts, J. J. (Royal Cancer

Hosp., London) and G. P. Warwick. Biochem. J. 87(1):14P, 1963.

β -Propiolactone, a mutagen and carcinogen, reacted almost quantitatively with guanosine, yielding 7-carboxyethylguanine or hydroxypropionylguanine on acid hydrolysis. Deoxyguanylic acid yielded the same product overnight at 37°C. In alkylated DNA the molar ratio of guanine:adenine was 0.1 (control = 0.7) after treating 10 μ g of DNA with 100 mg β -propiolactone at pH 7.2 for 24 hr. Bromoacetic acid reacted with deoxyguanylic acid to yield 7-carboxymethylguanine. Isolation of proteins and nucleic acids from Krebs ascites cells treated with bromo(C^{14})acetic acid revealed a preferential binding to protein, the specific radioactivity being 20 x that of the DNA fraction.

63-644 CONTROLLING THE MUTATION PROCESS IN CANCER CELLS. (Rus.) Dubinin, N. P. (Inst. Biol. Phys., Acad. Sci. USSR), L. V. Cherezhanova and E. K. Bulochnikova. Dokl. Akad. Nauk SSSR 146(4):917-920, 1962.

After *in vitro* exposure of Ehrlich ascites carcinoma cells (70-100,000/mm³) to streptomycin (ST) for 2-4 hr., the incidence of chromosomal rearrangements (bridges, fragments and rings) was determined 26 hr. after i.p. inoc. into mice. After ST (0.001-0.1 μ g/ml), incidence of chromosomal rearrangements at anaphase in daughter cells was 1.6% (1.2-2.4%); controls 0.0% (3.4-6.3%). Exposure to high concentrations of ST (10-50 mg/ml) had no effect on the number of mutations in the first mitoses (4.1-4.2%), but significantly increased the number of chromosomal rearrangements found after the 2nd and 4th mitoses (12.2-12.4% at 50 mg/ml compared to 1.7-2.5% in controls). It is suggested that the antimutagenic effect of ST and other compounds may be of use in preventing the transformation of precancerous conditions into frank malignancy.

63-645 THE EFFECT OF NEUROTIZATION ON THE DEVELOPMENT AND COURSE OF INDUCED MAMMARY TUMORS IN RATS. (Uk.) Lo Sing-Mao, A. Bogomolets Inst. Physiol. Acad. Sci., USSR, Kiev). Fiziol. Zh. (Kiev) 8(5):664-670, 1962.

3-4-month-old female rats made neurotic (NR) by a modification of the technic of Kozhevnikova, min. of 9,10-dimethyl-1,2-benzanthracene (DMBA; total dose 13 mg, i.v.) caused 15/16 (94%) to develop mammary tumors, 62% were adenocarcinomas, 38% stercarcinoma, and papillary or solid cancers; the av. number of tumors/rat was 3.5. Comparable figures for 22 rats which received DMBA only were 10%, 35% and 2.6. In groups of 15 which were ovariectomized and given DMBA, and in 15 treated similarly but with the addition of neurotization, mammary tumors appeared. In many of the

DMBA + NR rats there was prolongation of the estrus cycle and 62% (11/16) experienced dilation of the uterus with hemorrhage, compared to 12% in NR only rats. It is concluded that neurotization enhances the development of tumors in DMBA-treated rats, but only in the presence of ovarian hormones.

63-646 AN EXPERIMENTAL MODEL OF LEUKEMIA IN RATS AND MICE BY MEANS OF 9,10-DIMETHYL-1,2-BENZANTHRACENE. (Rus.) Semenskaia, E. M. (Inst. Exptl. Clin. Surg. Haematol., Acad. Sci. Gruz. SSR, Tbilisi), I. I. Abakeliia, E. Sh. Kiguradze and N. G. Larionova. Soobshch. Akad. Nauk Gruz. SSR 24(5):601-606, 1963.

Instillation into the bone marrow of 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.3 mg, in benzene) led to the death of 9/20 mature, stock rats due to embolism or general intoxication during the first few days. After 2 days most survivors showed a decrease in Hb (5-10%), RBC (500,000-1,600,000) and WBC (2,000-7,000); blood composition began to return to normal by day 10 and was complete by day 80. Leukocytosis (from 17,000 up to 42,000 by day 30) was seen among 7 rats, with gradual return to normal over periods of 20-120 days; 2 rats showed no changes. These results showed that DMBA in stock rats caused only a prolonged reaction in the peripheral blood without causing systemic disease. After 3-4 mo., only benign growths (on the ears and dorsum) were observed; there was no systemic change or tumor at site of inj. After s.c. inj. of DMBA into the dorsum (no details) of 11 stock mice, repeated hematological studies were made of 6 survivors. One mouse after 15 days showed WBC increase from 2,000 to 22,000 with myelocytes and hemocytoblasts present; this mouse died after 33 days with grossly enlarged spleen and lymph nodes while microscopically liver, lung and spleen showed myeloid infiltration. In the other mice there was a variable pattern as regards increase in WBC but increase in size of spleen and lymph nodes with myeloid infiltration was common. One mouse developed a rapidly growing tumor in the dorsum. In a further experiment an extract of spleen and lymph nodes of one mouse was given s.c. into the dorsum of two 5-month-old stock mice (male). After 15-21 days a typical picture of leukemia was noted with an increase in WBC to 32,000-46,000, appearance of hemocytoblasts and myeloblasts, spleen and lymph nodes were enlarged and in one mouse a tumor was found.

63-647 THE ROLE OF PHOTOPRODUCTS OF TYROSINE AND TRYPTOPHAN IN THE DEVELOPMENT OF LIGHT-INDUCED CANCER IN ALBINO MICE. (Ger.) Wetzel, R. (Res. Centre Med. Biol. Berlin-Buch, Ger. Acad. Sci.) and L. Lindigkeit. Arch. Geschwulstforsch. 20(2):85-95, 1963.

Several groups of albino mice received UV locally, 5-6 x/wk. until death, with radiation focused

on a shaved dorsal area. Mice receiving tryptophan prior to each exposure (1 ml of a 0.5% solution in saline, s.c. to the irradiated site) showed no significant differences of response, as compared to non-medicated controls. However, all mice receiving tyrosine in the same doses, in the same vehicle, developed sarcomas within a period of 5-10 mo. Among the mice receiving the vehicle alone, 2/10 developed sarcomas in 5 and 15 mo., resp. Also reported is the derivation *in vitro* of a number of photoproducts of both tryptophan and tyrosine; 3 of which were identified tentatively as oxylindole lactic acid, oxyskatol, and oxyindole. The authors conclude that the increased incidence of UV-induced tumors in animals treated with tyrosine or NaCl was due to non-specific reaction to irritation at the site of inj. and did not imply the involvement of any carcinogen.

- 63-648 EFFECT OF TESTOSTERONE AND OF ESTROGENS ON THE APPEARANCE OF EXPERIMENTAL TUMORS INDUCED BY 20-METHYLCHOLANTHRENE. (It.) Pannella, A. (Inst. Clin. Surg., U. Pavia, Italy) and G. Gasbarrini. *Arch. Pat. Clin. Med.* 39(3):198-218, 1963.

Female albino rats treated with estradiol benzoate (i.m. equivalent to 1000 I.U./day) from the time of the inj. of 20-methylcholanthrene (MC; 5 mg i.m. x 1) developed tumors earlier than non-estrogen-treated, MC-injected controls. In the estrogen treated group of 20 rats, median time of tumor appearance was 139 days, with 2/20 tumors appearing on day 97; in the MC control group of 25 rats median time was 165 days, with 6/20 tumors developing on day 139. Bilateral ovariectomy 20 days before MC inj. prevented the appearance of tumors in 10/10 rats, while admin. of testosterone propionate (i.m., equivalent to 2.5 mg/day) resulted in only 3/20 tumors, all appearing at day 139. All tumors were polymorphocellular sarcomas. Histochemical studies revealed increased tumor and muscle glycogen in estrogen-treated rats, and decreased glycogen in the tissues of those treated with testosterone.

- 63-649 GENETIC AND BIOCHEMICAL STUDIES OF THE SIGNIFICANCE OF AMINO AND NUCLEIC ACIDS IN PRIMITIVE NEOPLASTIC STRUCTURES (TUMORS AND GALLS). A PHENOMENON INVOLVING LONG-LASTING MODIFICATION AND/OR TRANSMISSIBLE MUTATION. (Ger.) Anders, F. (Zool. Inst., U. Saarland, Saarbrücken, Germany), F. Drawert, K. Klinke and K. H. Reuther. *Experientia* 19(4):219-224, 1963.

When experimentally developed hybrids of *Platy-poecilus maculatus* and *Xiphophorus helleri* (viviparous platyfish and swordtails) were maintained in dilute sea water (0.25-0.5% salt conc.), free amino acid levels were increased markedly within a few hr.; the growth of macro-melanophores was abnormally accelerated within

3-10 days; and their transformation into melanoma was completed within 3-8 mo. Return of the fish to fresh water was followed within a few hr. by reversion of amino acid levels to normal, but the accelerated growth and transformation phenomena continued autonomously. Cultivation of the mother fish under similar conditions for some weeks, while the young were still in an oocytic or embryonic state, induced the same phenomena in young which were born and maintained in fresh water; this appears to confirm the presence of an irreversible somatic mutation transmitted to succeeding daughter cells in the treated animal and resulting, in the young, in activation of a latent hereditary predisposition. The phenomenon continued to occur in offspring conceived subsequently, showing a progressively increasing latency period through the 9th group conceived, with disappearance thereafter. In a parallel study, the authors also note that canceriform plant galls induced in the leaves of certain species of grape vine by inj. of a concentrated mixture of amino acids into the meristems (experimentally, or by the use of a parasitic insect, *Phylloxera vastatrix*) continue to grow at a constantly decelerating rate for at least 12-14 days after the source of increased amino acid is removed; that even very small inj. of amino acids into the meristem are followed within a few hr. by a significant increase of RNA concentration in the leaves which will eventually bear galls; and that the deceleration of post-inj., autonomous growth of the induced galls is paralleled by a reduction of RNA levels in the affected leaves, with return to normal by the time growth has ceased. The authors suggest that RNA (and, therefore, protein) biosynthesis in all neoplasms may be similarly dependent on concentration levels of free amino acids.

- 63-650 AN EARLY TEST FOR POSSIBLE SKIN CARCINOGENS IN THE MOUSE: EFFECTS OF A BENZACRIDINE AND OF SOME TRICYCLOQUINAZOLINES. (E.) Iversen, O. H. (Inst. Gen. Exptl. Path., U. Oslo, Norway). *Nature (London)* 198:400, 1963.

The possible specificity of the tetrazolium reduction method for identification of skin carcinogens was further supported by blind tests using tricycloquinazoline and its 3-methyl carcinogenic derivative, as well as the non-carcinogenic 2-methyl derivative. The first 2 compounds gave tetrazolium test results of 1.310, while the last compound gave a test result of 0.874.

- 63-651 ACTION OF VAGOTOMY ON THE NEOPLASTIC LESIONS OF GLANDULAR STOMACH PRODUCED IN MICE BY 20-METHYLCHOLANTHRENE. (E.) Vilchez, C. A. (Fac. Med., Natl. U. Cuyo, Argentina) and J. M. Echave Llanos. *Naturwissenschaften* 50(7):305-306, 1963.

Following unilateral vagotomy, 26 female, 180-day-old, C57L mice received 20-methylcholanthrene (20-Me; 0.3 mg in 0.01 ml aqueous suspension

f gum arabic) by inj. into the submucosa of the anterior wall of the glandular stomach. When sacrificed 60 days later, 13/26 had neoplastic lesions which were limited to the mucosal layer; 1 had lesions invading the muscularis propriae; and 2 had lesions invading the peritoneum. In a group of 26 unoperated animals which received 20-Me in the same way, results were 2, 13, and 11, resp. Two of the vagotomized animals had 2 developed tumors, each; while 4 of the unoperated animals had 2-4 developed tumors, each. There were no significant histologic differences between the 2 groups; and no neoplastic lesions were found in 3 additional control groups consisting of animals sham-inj. post vagotomy, sham-vagotomized, or sham-inj. only. The authors conclude that vagotomy tended to diminish or retard the invasiveness of the 20-Me-induced neoplasia under study, although the mechanism of action was considered unclear.

652 GLYCOLYTIC ENZYMES AND THEIR RELATIONSHIP TO HEPATOMA AND DIABETES. Heise, (Robert-Rössle-Clin. Germ. Acad. Sci., Berlin) and M. Görlich. Neoplasma (Bratisl.) 1(1):17-30, 1963.

In 3 lots of liver homogenates derived from animals bearing hepatoma induced by feeding methylaminoazobenzene, 5 mg/day x 200, fructose-1,6-diphosphatase (FDP-ase) content was reduced ($\mu\text{M PO}_4/\text{mg/hr.}$) from 214-151, 284-153, and 240-116, resp., as compared to liver homogenates derived from normal controls. In the 3 lots, glucose-6-phosphatase content was reduced from 194-84, 182-42, and 186-118, resp., compared to homogenates derived from normal controls. Proteolytic activation of homogenates derived from hepatoma-bearing rats by means of incubation with varying amounts of trypsin at 37°C , resulted in a mean decrease of FDP-ase content of 22.2% (range, -10 to -48.6%) in contrast to a mean increase of 99.5% (range, 1.5-158.0%) in those derived from normal controls. The authors suggest that during the long process of cancer development, the carcinogen may attack enzyme molecules directly, in such fashion as to deactivate them; and that although this process may be temporarily compensated by increased liberation of enzyme molecules within an organism, such increased liberation eventually reaches a maximal plateau level, followed by increased total enzymatic deactivation due to a continued activity of the carcinogen.

653 RELATION BETWEEN SENSITIVITY TO LACROGENIC HORMONES AND TUMORIGENESIS IN HYPERPLASTIC MAMMARY NODULES IN C3H/Crgl MICE. Bern, H. A. (Cancer Res. Genetics Lab., Cal., Berkeley). Proc. Soc. Exp. Biol. Med. 112(4):864-866, 1963.

Pregnant, multiparous C3H/Crgl mice bearing hyperplastic mammary alveolar nodules were

treated s.c. with cortisol acetate (50 μg , 50 μg , or 75 $\mu\text{g}/\text{day} \times 3$, 5, and 3, resp.); or corticosterone acetate (500 μg , 1,000 μg , or 1500 $\mu\text{g}/\text{day}$, all $\times 3$); or deoxycorticosterone acetate (1,000 $\mu\text{g}/\text{day} \times 5$ or 1500 $\mu\text{g}/\text{day} \times 3$); or 17 β -estradiol (by implant of 1 mg or 2.5 mg pellets; duration of treatment, 10 days). For test of tumorigenesis, the fat pads of 127 virgin 3-week-old female mice were cleared of all mammary parenchyma. Nodules which showed some milk secretion were transplanted into 1 side of the inguinal mammary fat pads and nodules which showed little or no milk secretion, into the pads on the other side. There was no significant differences between the 2 types of nodules as far as tumorigenesis was concerned (tumors formed in 33% of "milk secreting" nodules and in 27% of the "non-milk-secreting" nodules).

63-654 THE ETIOLOGY OF CANCERS OF THE BLADDER. (Ger.) Röhl, L. (Surg. Clin., Ruprecht-Karl-U., Heidelberg, Germany). Urologe 2(2):57-61, 1963.

In a review (12 references) of the effects of the direct contact of urine with the mucosa of the bladder, the author states that several aminophenolic carcinogens (e.g., 1-hydroxy-2-naphthylamine, 3-hydroxyanthranilic acid, 3-hydroxykynurenine), which are inactivated in the liver by being bound to glucuronic acid, can be freed again in the bladder by β -glucuronidase--a substance which shows increased levels of activity in a significantly high percentage of pts. with carcinoma of the bladder, but not in pts. without bladder tumors. Several bladder mucosa and tumor tissue cultures (TC) were made in a combination with chick embryo extract, chicken plasma, human serum, lysine ethylester, and 2.5 $\mu\text{g}/\text{ml}$ of 3-hydroxyanthranilic acid (HAA). A mean TC control value (without HAA) of β -glucuronidase activity (GLA; in U/ml) was 2.0. In TC's with HAA, GLA of tumor plus mucosal tissue from 2 pts. with undifferentiated carcinoma of the bladder was 0.87 and 4.28 U/ml, resp. Taking the mean growth rate of TC controls as 100, the growth rates of tumor samples were 102.2 and 190.1, resp.; growth rate of the normal mucosa was 92.9 and 179.2, resp. For normal mucosal tissue (only) from a 2nd pt. with papilloma of the bladder, GLA was 1.18 and growth was 89.4; while for tumor tissue from a 3rd papilloma pt., GLA was 2.76 and growth was 109.3. GLA and growth were also tabulated for tumor tissue only taken from 3 pts. with undifferentiated carcinomas of the bladder and values were, resp.: 2.09 and 83.5; 2.86 and 76.3; 3.14 and 134.7. GLA of tumor tissue in a pt. with papilloma was 8.0; tumor and mucosal TC in the same pt. showed growth rates of 103.9 and 69.2, resp. The author concludes that additional tissue culture studies of the possible effects of carcinogenic substances in the urine appear to be warranted.

- 63-655 SPECIAL FEATURES OF LIVER REGENERATION IN MICE DURING THE COURSE OF EXPERIMENTAL CARCINOGENESIS. (Rus.) Gel'shtein, V. I. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). Vop. Onkol. 9(4):61-67, 1963.

The skin of 277 C₃HA mice was painted 20 x in 7 wk. with o-aminazotoluene (1% in benzene). After intervals ranging from 1-360 days, the animals were subjected to partial hepatectomy, 48 hr. after which they were sacrificed. Mortality in the treated mice was 150/277 (54.2%), as compared to controls, 20/120 (16.7%). When hepatectomy was performed 1 day after treatment, 15/16 died; when performed 7 days after treatment, 9/15 died. Among the survivors, the lowest mortality was 11-12% on day 300, and 31-32% on day 360. The mitotic activity of hepatic cells decreased up to day 45 after treatment + hepatectomy. On day 60 the mitotic activity increased about 7x with simultaneous appearance of adenomatous nodes of basophilic hepatic cells. On day 200, due to the conglomeration of the nodes, the degree of dystrophy and the distribution of mitotic figures decreased. Malignant tumors developed only in isolated cases. The av. mitotic coefficient in the nodes was 0.54% before surgery, and 31.68% after surgery.

- 63-656 FAILURE OF PHENOXYBENZAMINE TO PREVENT FORMATION OF HEPATOMAS AFTER CHRONIC CARBON TETRACHLORIDE ADMINISTRATION. (E.) Kiplinger, G. F. (Boston U. Sch. Med., Mass.) and C. J. Kensler. J. Nat. Cancer Inst. 30(4):837-843, 1963.

In male C₃H mice, 2-4 mo. old and weighing 25 g, Dibenzylamine (phenoxybenzamine; 2.0 and 4.0 mg/kg, i.p.), given concurrently over 10 wk. with intragastric CCl₄ (0.2-1.6 g/kg in corn oil; 3x/wk. x 10) failed to protect against CCl₄ toxicity or against the formation of hepatomas. In acute experiments, however, 4.0 mg/kg, i.p. 30 min. before CCl₄ (intragastric, 2.5 g/kg) gave complete protection against increased deposition of lipids in the liver. At 8.0 mg/kg, no protection occurred, indicating a biphasic dose-response curve. Reserpine (0.5 mg/kg i.p. in acidified aqueous soln.) also protected against lipid deposition, although to a less marked degree. Ergotamine (3.0 mg/kg, i.p. in aqueous soln.) afforded only partial protection; 6.0 mg/kg increased lipid deposition significantly. Mannitol hexanitrate (0.5-2.0 mg/kg, i.p.) was entirely ineffective; and ephedrine sulfate (2.0 mg/kg) potentiated the toxic effect of CCl₄ on liver lipid content.

- 63-657 INFLUENCE OF DOSE AND AGE ON THE INDUCTION OF MALIGNANT LYMPHOMAS AND OTHER TUMORS BY 7,12-DIMETHYLBENZ(α)ANTHRACENE IN SWISS MICE. (E.) Toth, B. (Div. Oncol., Chicago Med. Sch., Ill.), H. Rappaport and P. Shubik. J. Nat. Cancer Inst. 30(4):723-741, 1963.

Of 75 Swiss mice which received 9,10-dimethyl-1,2-benzanthracene (75 μg, s.c. in tri-n-caprylin x 1) at birth, 5 females and 13 males survived to weaning; 1 and 2, resp., to wk. 30; and 0 and 1, resp., to wk. 40. The number reported as developing malignant lymphomas up to wk. 35 was 4 and 4, resp. (tabulated as 80% and 40%, resp.); pulmonary tumors, 5 and 12 (100% and 100%, resp.); s.c. sarcomas, 1 and 1 (33.3% and 14.2%, resp.). Two papillomas of the forestomach were also found. At dose levels of 50 μg or below, the reported incidence of malignant lymphomas dropped sharply; increasing the dosage to 100 μg decreased the incidence in females developing this disorder by wk. 35 from 80% to 50.3%. In males given 100 μg, incidence increased from 40.0% to 63.6%. Animals 2-4 wk. old were reportedly significantly less susceptible to the carcinogen. Undifferentiated (stem cell) malignant lymphomas were invariably thymic, and found only in treated animals. Lymphocytic, histiocytic, and lymphohistiocytic lymphomas were primarily non-thymic, and occurred in both treated and untreated mice. The incidence of s.c. sarcomas at the site of inj. increased with larger doses and advancing age of survivors.

- 63-658 CHROMOSOMES OF PRIMARY GRANULOCYTIC LEUKEMIA (CHLOROLEUKEMIA) IN THE RAT. (E.) Nowell, P. C. (Dept. Path., U. Penna. Sch. Med., Philadelphia), S. Ferry and D. A. Hungerford. J. Nat. Cancer Inst. 30(4):687-703, 1963.

Chromosome studies of the bone marrow (sometimes spleen and lymph nodes) were done on 9 rats with primary granulocytic leukemia induced by gastric instillation of 20-methylcholanthrene. Significant deviations from the normal diploid number were observed in only 1 rat whose leukemic cells showed at least 2 abnormal stemlines, with 43 and 44 chromosomes, instead of 42. The other 8 rats with chloroleukemia, and 3 with primary lymphocytic leukemia (also induced by 20-methylcholanthrene), did not show chromosome changes. A transplantable chloroleukemia carried for 10 yr showed an apparently stable abnormal stemline with 43 chromosomes.

- 63-659 THE DELETION OF KYNURENINE HYDROXYLASE ACTIVITY DURING HEPATOCARCINOGENESIS. (E.) Kizer, D. E. (Samuel Roberts Noble Found., Inc., Ardmore, Oklahoma) and B. A. Howell. J. Nat. Cancer Inst. 30(4):675-686, 1963.

Mitochondria from 4 transplanted rat hepatomas, and 2 transplanted mouse hepatomas, and from primary hepatomas induced in rats by 4-dimethylaminoazobenzene (DAB), 3'-methyl-DAB and 4'-fluor DAB failed to show any kynurenine hydroxylase activity. The absence of enzyme activity was not associated with endogenous inhibitors or with the absence of essential activators in whole or

uble fraction mitochondria isolated from nor-liver. Also ineffective were several compounds which were possible activators or cofactors of kynurenine hydroxylase. The kynurenine hydroxylase activity of rats maintained on a basal riboflavin deficient diet, or this diet + 0.06% 4'-methyl-DAB or basal diet + 0.06% 3'-methyl-DAB, were as follows: control, 0 wk., 0.51; 4 wk., 0.32, 0.14 and 0.14; 8 wk., 0.46, 0.27 and 0.19 and 12 wk., 0.51, 0.31 and 0.19 (in μM 3-hydroxykynurenine/mg protein/90 min.), suggesting that in precancerous livers the heaviest losses are in the group fed 3'-methyl-DAB, then in that receiving 4'-methyl-DAB, and least in the group on the riboflavin deficient diet.

660 THE TRANSFORMATION OF THE LIVER PARENCHYMAL CELL INTO A CANCER CELL. (CARCINOGENESIS AS A PROGRESSIVE TRANSFORMATION OF LIVER CELLS) (Ger.) Oehlert, W. (Inst. Path., Freiburg i. Br., Germany) and J. Hartje. *Zurichwissenschaften* 50(9):358-359, 1963.

A brief preliminary report on the results of autoradiography following admin. of tritiated cytidine (H^3 -cytidine) to rats at varying doses during the induction of hepatocellular carcinoma by the feeding of diethylnitrosamine (5 mg/day for 120-150 days), the authors point out that the loss of cytoplasmic basophilia during carcinogenesis is accompanied by a disproportionate increase in nuclear RNA synthesis and a decrease in the nucleoprotein content of the cytoplasm; after the development of a carcinoma, the cytoplasmic RNA is increased but nuclear RNA synthesis continues to be elevated, although protein synthesis is depressed during both of these periods. With respect to the mechanism of carcinogenesis, the authors theorize that the alkylation of guanine in the RNA results in decreased protein synthesis and a consequent loss of structural proteins, which then leads to decreased cytoplasmic RNA but a stimulation of DNA synthesis, since this is normally inhibited by the proteins. This DNA synthesis takes place in the presence of abnormal nucleotides from the RNA, resulting in transmission of mutations and eventually in abnormal cytoplasmic RNA and proteins, which lose their specificity. See also CRA 1(1):#6 and *ibid.*, (2):#211, 1963.)

661 EFFECT OF CARCINOGENIC POLYNUCLEAR HYDROCARBONS ON CORTICOSTERONE AND ASCORBIC ACID CONTENT OF ADRENAL GLANDS IN RATS. (U.S.) Dao, T. L. (Roswell Park Mem. Inst., Buffalo, N.Y.), B. Flaxman and P. Lonergan. *Proc. Soc. Biol. Med.* 112(4):1008-1012, 1963.

Male Sprague-Dawley rats 50-55 days old received intragastrically (in olive oil) 9,10-dimethyl-1,2-benzanthracene (DMBA; 20 mg) or 20-methylcholanthrene (20-Me; 30 or 60 mg). The mean adrenal corticosterone conc. ($\mu\text{g/g}$ adrenal wt.) on day 1, 2, 4, 5, 6, 8, 15, 20, and 25 for DMBA-fed rats was 33.5, 27, 17, 14.6, 12, 12.5, 21.9, 28.3,

51.5, and 25, resp.; that for 20-Me (30 mg) fed rats was 34, 22, 19.4, 13.8, 19.6, 21, 27.3, 28, 31.4, and 29.8 resp.; that for 20-Me (60 mg) fed rats was 43.2, 21.5, 18, 14.4, 15, 14.4, 23.2, 36.6, 33.6, and 30.7, resp., as compared to untreated controls which ranged in 25 days from 23.8-30.2, and 18.6-26.3 in olive oil fed controls. The decline in adrenal corticosterone conc. was correlated in DMBA-fed rats with necrosis and hemorrhage; the rise with calcification which began on the 6th day and regeneration which was completed on the 15th day. No necrosis was observed in the 20-Me fed rats. The serum corticosterone conc. followed the adrenal pattern within the 25 day period ranging for DMBA rats, from 11.6-50 $\mu\text{g}/100\text{ ml}$ serum; for 20-Me (30 mg) rats, 19-48.6; and 17.6-31.8 and 20.6-34.8 for olive oil fed and untreated controls, resp. In DMBA-fed rats adrenal ascorbic acid conc. declined on the 2nd day and remained at a low level; in 20-Me fed rats it rose on days 1-5 and then dropped to normal values. The conc. of plasma ascorbic acid was not altered by the carcinogens. The suppression of corticosterone synthesis by DMBA is believed to be secondary to tissue damage; since 20-Me did not induce any morphological change it appears that these 2 carcinogens act in different ways.

63-662 CARCINOGENIC EFFECT OF EGG WHITE, EGG YOLK AND LIPIDS IN MICE. (E.) Szepeswol, J. (U. Puerto Rico Sch. Med., San Juan). *Proc. Soc. Exp. Biol. Med.* 112(4):1073-1076, 1963.

Incidence of malignancy in T.M. nonbreeding mice maintained from the age of 4 wk. on Rockland Diet (RD), RD supplemented with hard boiled egg white (RDW), supplemented with raw egg yolk (RDY), or with cholesterol and lard (RDC) was 1/20, 18/20, 19/21, and 9/19, resp. The incidence of lung adenocarcinomas for RD, RDW, RDY and RDC was 1/20, 10/20, 14/21, and 6/19, resp.; that for lymphosarcomas 0/20, 17/20, 15/21, and 1/19, resp. Mammary cancers did not develop in any case. In a similar experiment where the mice were allowed to breed for 3-4 generations and the offspring were maintained on the same diets, incidence of malignancy for RD, RDW, RDY and RDC were 16/97, 130/152, 121/139, and 67/140, resp.; that for lung adenocarcinoma was 10/97, 60/152, 57/139, and 26/140, resp.; that for lymphosarcomas 2/97, 110/152, 98/139, and 5/140, resp.; and that for mammary cancer 0/97, 0/152, 23/139, and 37/140, resp., appearing in 2-4 generations. Lung adenomas were large in RDW and RDY mice and developed at an earlier age compared to controls. When 4-6 week old RDY and RDC mice of the 3rd and 4th generation were put on RD, 8/9 and 22/35, resp., developed malignancies. Of breeding females on RDY, 23/69 developed mammary cancer, 0/68 on RDW. A carcinogen causing development of lung adenocarcinomas and lymphosarcomas is believed to be present in both egg white and yolk. The mammary gland carcinogen (present only in yolk) apparently is a lipid material. The TM strain is considered cancer resistant, and in 15 yr. of inbreeding the mice have rarely developed malignancies.

- 63-663 EFFECT OF SEVERAL DRUGS AND CHEMICALS ON HEPATIC GLUCURONIDE FORMATION IN NEWBORN RATS. (E.) Arias, I. M. (Albert Einstein Coll. Med., New York), L. Gartner, M. Furman and S. Wolfson. *Proc. Soc. Exp. Biol. Med.* 112(4): 1037-1040, 1963.

O-Aminophenol glucuronide (OAPG) and direct acting bilirubin formation in pregnant and newborn Wistar rats was estimated in liver homogenates. Both were increased 2-4 x after admin. of 3,4-benzpyrene (BP, 1 mg/day x 3, i.p.) or chloroquine (CQ, 0.5 mg/day x 3). BP (2 mg/day) admin. 10 days prior to parturition doubled OAPG formation in maternal liver but had no significant effect on neonatal liver; CQ (25 mg/day) increased maternal and neonatal OAPG formation 1.5 x. CQ (50 mg/wk. to women 1-8 wk. before delivery) did not significantly alter daily serum total bilirubin conc. in infants. Chlorcyclizine, (CZ, 1 mg/day x 3) and pamaquine (0.5 mg/day x 3) increased OAPG and direct acting bilirubin formation; CZ admin. to rats 10 days prior to parturition increased maternal and neonatal OAPG formation.

- 63-664 EFFECTS OF THIOACETAMIDE ON INCORPORATION OF OROTIC ACID-2-C¹⁴ INTO RNA FRACTIONS IN LIVER. (E.) Adams, H. R. (Baylor U. Coll. Med., Houston, Texas) and H. Busch. *Cancer Res.* 23(4):576-582, 1963.

The amounts of p-RNA (released by phenol in the aqueous phase) and r-RNA (remained in phenol) were increased 2-3 fold in the nuclei of rat liver cells after i.p. admin. of thioacetamide (50 mg/kg/day x 9) to albino male rats. Other changes were a 2-fold and 3.5-fold increase in nucleolar p-RNA and r-RNA, resp.; a decrease in microsomal and mitochondrial RNA and an increase in p-RNA of the cytoplasmic sap. Thioacetamide suppressed the incorporation of orotic acid-2-C¹⁴ (3.3 μ C/rat i.v.) into the p-and-r-RNA of nucleus and cytoplasmic sap when measured as specific activity; nucleolar p-RNA was unchanged, but r-RNA was decreased 30%.

- 63-665 THE MORPHOLOGY OF THE PULMONARY TUMORS PRODUCED BY INTRAVENOUS INJECTION OF NITROSOMETHYLURETHAN IN THE RAT. (Ger.) Thomas, C. (Inst. Path., Rheinische Friedrich-Wilhelms U., Bonn, Germany) and D. Schmähl. *Zschr. Krebsforsch.* 65(4):294-302, 1963.

Admin. of nitrosomethylurethan (1 mg/kg i.v. every 10 days, total dose 40 mg/kg) to BDX rats for 400 days resulted in pulmonary tumors in 18/20 animals (work reported by Druckrey et al., *Naturwissenschaften* 49:451, 1962); these rats were then sent to the present authors for histological study. Macroscopic examination revealed

multiple, sharply delineated, greyish nodules in several lobes per animal, with a progression of histological changes from focal proliferation of alveolar epithelium near the intermediate arteries to micro-infiltrations of round cells, adenomas, transitional adenoacanthomas and various other types of carcinoma; most of the tumors, however, were benign, with no metastases. The most common malignancy was alveolar cell carcinoma followed by cornifying squamous cell carcinoma, both of which had their origin in the peripheral parenchyma and were often seen in close proximity with transitional forms between them resembling adenoacanthoma, while the adenocarcinomas and adenoacanthomas proper arose from the large bronchi and were characterized by large amounts of collagen. There was frequent tumor necrosis and calcification, and the tumor-free areas of the lung often showed connective tissue proliferation, ossification and inflammatory infiltration. In addition, 2 animals showed renal carcinoma, which was also assumed to be due to direct contact with the active carcinogen, and 1 showed an ovarian carcinoma, which may well have been spontaneous.

- 63-666 EXPERIMENTAL STUDIES ON "SYNCARCINOGENESIS". I. EXPERIMENTAL PRODUCTION OF CANCER IN RATS BY THE SIMULTANEOUS ADMINISTRATION OF DIETHYLNITROSAMINE AND 4-DIMETHYLAMINOAZOBENZENE. (Ger.) Schmähl, D. (Inst. Path., Rheinische Friedrich-Wilhelms U., Bonn, Germany), C. Thomas and K. König. *Zschr. Krebsforsch.* 65(4):342-350, 1963.

In a comparative study of the carcinogenic effect of orally admin. diethylnitrosamine (DENA) and 4-dimethylaminoazobenzene (DAB) in 2-3 month-old male and female rats, cancer of the liver was produced in all 28 rats given DENA alone (3 mg/kg p.o. = 1/70 of the LD₅₀), after a median induction time of 233 days and a total dose of 700 mg/kg. After DAB alone (33 mg/kg/d p.o. = 0.1 LD₅₀), 18/23 developed liver cancer after a median induction time of 235 days and a total dose of 7770 mg/kg. Admin. of both DENA and DAB at the same dosages for a median total dose of only 460 mg/kg DENA and 5160 mg/kg DAB resulted in liver tumors in 36/38 after a median induction time of 153 days; after DENA at the original dosage plus compression of 1 lobe of the liver 2 times in 4 w (mean induction time of 252 days and total dose 755 mg/kg), 14/19 developed tumors. In all cases treatment with the carcinogen was stopped after the first palpable nodule developed, and the rats died an av. of 28 \pm 10 days later. Autopsies revealed multicentric foci of liver cancer with metastasis to the mesentery, omentum and occasionally the liver, and sometimes bloody ascites. Histologically, benign hepatomas, adenohepatoma, type I hepatocellular carcinoma and adenocarcinoma were seen, the latter sometimes surrounded by sarcomatous stroma formation. All of the malignant tumors in rats fed DENA alone, with or without compression of the liver (which had no significant effect), were hepatocellular carcinomas;

these rats also showed periportal fibrosis, and in those in which the liver was compressed, all the tumors arose from the normal parenchyma. Hepatocellular carcinoma was also the most common malignancy in rats given DAB or DAB + DENA, but now there were also some adenocarcinomas, cystadenomas and pseudo-bile-duct proliferation; in contrast to the rats given DENA alone, those given DAB showed poor wt. gain. The authors conclude that DENA and DAB have an additive effect and that both act on the same type of liver cell.

63-667 THE EFFECT OF OLFACTORY LOBECTOMY AND INDUCED PSEUDOPREGNANCY ON THE INCIDENCE OF METHYLCHOLANTHRENE-INDUCED MAMMARY AND OVARIAN TUMOURS IN C3Hb MICE. (E.) Biancifiori, P. (Div. Cancer Res., U. Perugia, Italy) and F. Caschera. *Brit. J. Cancer* 17(1):116-118, 1963.

The incidence of mammary tumors in 30 lobectomized, 10 virgin, and 30 pseudopregnant C3Hb mice after 10-methylcholanthrene (1 mg/wk. x 8, p.o.) was 9%, 33%, and 78%, resp. No tumors occurred before week 40 in lobectomized mice, whereas 3/10 virgin and 20/23 pseudopregnant had developed mammary tumors. Multiple tumors occurred only in 4/23 pseudopregnant mice. In lobectomized mice, pseudopregnancy was abolished; in virgins, 4% of the cycles were pseudopregnancies; and in females mated with vasectomized males, pseudopregnancy developed in 46%. Ovarian tumors occurred in 11/26 of lobectomized mice; 5/24 of virgins; and 4/16 of pseudopregnant mice. (See also CRA 1(2):#201; *ibid.*, (4):#629, 1963.)

63-668 EXPERIMENTAL STUDY OF THE RELATIONSHIP BETWEEN VITAMIN B₁₂ AND TWO ANIMAL TUMOR SYSTEMS. (E.) Rigby, C. C. (Hosp. Sick Child., Great Ormond Str., London) and M. Bodian. *Brit. J. Cancer* 17(1):90-99, 1963.

Vitamin B₁₂ (5 µg/day x 8, s.c.) 1 day after serial transplantation of C1300 neuroblastoma to CAF1/Jax mice (100 series in 3 yr., 32 series in 1 yr.) led to decreased tumor growth (33%) and increased tumor vitamin content (90%). In a shorter series, tumors became extinct after 1 yr. Vitamin B₁₂ (30 µg/day x 5-7 wk.) after serial transplantation of PWA2-fibrosarcoma to August strain rats (15 series in 2 yr.) increased tumor growth 200% and vitamin content 55%. After Co⁵⁸-labeled vitamin (0.075 µg, s.c. to mice) the av. percentage of radioactivity of the inj. dose/g of wet tissue in mouse tumors 4, 24, 48, 72, and 96 hr. after inj. was 10.7%, 17%, 14.6%, 13.2%, and 12.8%, resp.; in rats given 0.2 µg, tumor content for the same time intervals was, 0.94%, 0.76%, 0.82%, 0.6% and 0.48%, resp. After 96 hr., the mouse tumors showed conc. much higher than those found in the spleen (4.7-5.1%) and similar to those found in the liver (12-14.8%) which is the storage organ in the mouse. The conc. in rat tumors was about the same as spleen (0.66-1.48%). In the mouse tumors, B₁₂ tumor conc. averaged 17.6 x that

of rat tumors. When B₁₂ activity was assayed by growth of *Lactobacillus leichmannii* 313, mouse tumors exhibited an increase of B₁₂ activity 5-6 x greater than brain or spleen; in rat tumors, increase was only 2-fold.

63-669 THE FATE OF EHRlich CELLS INJECTED INTO THE PORTAL SYSTEM. (E.) Koike, A. (Roswell Park Mem. Inst., Buffalo, N. Y.), H. Nakazato and G. E. Moore. *Cancer* 16(6):716-720, 1963.

Inj. of 10⁴, 10⁵, 10⁶, or 10⁷ Ehrlich ascites tumor cells (EATC; in 0.1 ml medium 199) into the portal vein of 6-8 week-old male Swiss mice produced liver metastases in 0/15, 27/81, 7/12, and 8/9, resp. After inoc. of 10⁵ EATC, viable tumor cells were present in the liver of 2/14 for at least 24 hr.; no cells were detectable after 7 days. Viable tumor cells that had passed through the liver were detected in the blood of 3/24 immediately after inoc., but not thereafter. No tumor implants were found in the lungs immediately after inj. or 24 hr. later. After manipulation of the liver, incidence of metastases was 39% on the 3rd day compared to controls, 33%. Viable tumor cells lodged in the liver appeared to be inactivated within 4 days. Cortisone acetate (2.5 mg s.c.) 1 day prior to or concurrent with EATC inoc. increased the number of mice with liver metastases (21/22 and 14/15, resp., controls, 13/44) and the number of metastases per mouse; treatment 1 or 2 days following EATC inoc. did not significantly change the number of mice with liver metastases but reduced the number of metastases. After cortisone treatment 1 day prior to inoc. with as few as 10 or 100 EATC, liver metastases developed in 3/19 and 6/14, resp., controls, 13/44. After total body (250 r) and local to liver (1,500 r) irradiation 3 days prior to EATC inoc., or CCl₄ (40% in mineral oil, 0.1 ml s.c.) or Thorotrast (0.2 ml, i.v.) 1 day prior to EATC inoc., metastases developed in 12/15, 9/10, 9/13, and 19/23, resp., compared with controls, 6/21. It is postulated that these agents interfere with the activity of a hepatic tumor-inhibitory factor.

63-670 STUDIES ON BONE MARROW. (PART 10). BEHAVIOR OF BONE MARROW IN THE DEVELOPMENT OF LEUKEMIA. (E.) Hiraki, K. (Dept. Med., Okayama U. Med. Sch., Japan). *Jap. J. Med.* 2(1):126, 1963.

In the preleukemic stage of 20-methylcholanthrene-induced myelogenous leukemia in Rf mice, a resemblance to hypoplastic anemia was noted in both peripheral blood and bone marrow, particularly the pattern of bone marrow in tissue culture. As the bone marrow became hyperplastic, leukemic cells began to enter the peripheral blood. When fluorescence antibody technics were applied to the study of viral leukemias in AKR and C58 mice, viral antigens appeared as fine particles or were grossly

aggregated; they were partly around the nuclear membrane and partly at the cytoplasmic margin of the leukemic cell. A few were observed intercellularly and some were scattered in the cytoplasm of the reticulum cell. It is postulated that leukemia viruses are produced intracellularly and are liberated extracellularly as they mature.

- 63-671 EFFECTS OF ADENALECTOMY AND HYPOPHYSECTOMY ON URINARY EXCRETION OF N-HYDROXY-2-ACETYLAMINOFLUORENE BY THE RAT. (E., Abstract) Lotlikar, P. D. (McArdle Memorial Lab., U. Wisconsin, Madison), E. C. Miller and J. A. Miller. Proc. Am. Assn. Cancer Res. 4(1): 39, 1963.

The excretion of N-hydroxy-2-acetylaminofluorene (N-HO-AAF), a major metabolite of 2-acetylaminofluorene (AAF) which has greater carcinogenicity in the rat than the parent compound, was studied in weanling adrenalectomized rats, admin. AAF 3 mg/100 g 5-10 days postoperatively. N-HO-AAF excretion was decreased by 60% compared to controls. Cortisone (2.0 mg/day) restored the N-HO-AAF excretion to 80% of normal, and cortisone + DOCA (2 mg each/day) permitted normal excretion. The excretions of 3-, 5-, and 7-HO-AAF by adrenalectomized animals were 90, 70 and 100% of normal, and were increased to 20, 15 and 50% above normal by cortisone admin. The same cortisone dose had no effect on the excretion of N-HO-AAF by intact rats. Hypophysectomy caused a decrease in N-HO-AAF excretion to 25-65% of normal. This was prevented partially by ACTH (2 U/days), and completely by Armour's growth hormone (Somat A; 2 mg/day). Soluble liver fractions from all animals revealed no differences in the reduction of N-HO-AAF to AAF in the presence of NADH or of NADPH, suggesting that the lower excretions after adrenalectomy or hypophysectomy are due to a decreased formation and/or conjugation of N-HO-AAF.

- 63-672 ALPHA-PARTICLE ACTIVITY AND FREE RADICALS FROM TOBACCO. (E.) Marsden, E. (Dominion Phys. Lab., Lower Hutt, New Zealand). Nature (London) 198:962-964, 1963.

In the course of work on the radioactivity of various crops grown on radioactive soils in certain countries, samples of cigarette tobacco leaf were examined and some samples were found giving total alpha activities (TAA) of 16 picocuries (pc.) per g of raw tobacco; some cigarettes were found which gave TAA as high as 4.4 pc./g. Total TAA and free radical production was measured using specially made cigarettes made with 2 types of S. American Brazilian tobacco and 2 of the Virginia type; conditions of pyrolysis were controlled, and smoke temperature was measured as 850°C. TAA (pc./g of raw tobacco) and total free radicals ($\times 10^{15}$ /g of smoke condensate), resp., for the 2 S. American types were 10 and 3.4; and 8.5 and 1.6. Values for the 2 Virginia types were 2.5 and 2.8; and 1.4 and 1.8. The amount of stable

free radicals (those which have a life in excess of 30 seconds at room temperature) were, in the same order: 1.5, 1.2, 1.0 and 0.8. It is conjectured that there will be considerable differences between tobaccos of different varieties or strains, and that the pick-up of α -active nuclei may be genetically connected. The author feels further examination of the effect of α -radiating nuclides in cigarette tobacco is called for either by direct effect or indirectly through radical production.

- 63-673 PRELIMINARY REPORT ON THE CELLULAR EFFECTS OF TRYPTOPHAN AND ITS METABOLITES UPON EHRlich ASCITES TUMOR. (E.) Yoshida K. (Mie Prefect. U. Sch. Med., Tsu, Japan), H. Oshima, T. Fukui and Y. Takatsuka. Mie Med. J. 12(1):35-38, 1962.

Anthranilic acid (AA, 2.0 mg/10 g, in saline, i.p.) 6-7 days after inoc. of Ehrlich ascites tumor cells into mice increased the number of mitotic cells in the tumors after the indicated hourly intervals as follows: 24, 3.12%; 48, 4.37%; 72, 4.17%; 96, 3.91%; and 120, 3.81%; compared with controls for the same time intervals, 3.26%, 2.69%; 3.08%; 3.03%; and 2.83%, resp. The lowest effective quantity of AA was 0.25 mg/10 g. Values for L-tryptophan (5 mg/10 g) for the same intervals were 3.34%; 4.66%; 3.55%; 3.71%; and 2.58%, resp. Those for kynurenine (2 mg/10 g) were 4.84%; 4.78%; 4.80%; 5.21%; and 3.32%, resp. Metabolites of tryptophan such as 3-hydroxyanthranilic acid, 5-hydroxyanthranilic acid, picolinic acid, nicotinic acid, and indol had no activity. The authors believe that AA is responsible for the stimulation of mitotic activity in the tumor cells.

- 63-674 EFFECT OF URETHANE ON PULMONARY TUMORS PRODUCED BY METHYLCHOLANTHRENE. (E.) Rigdon, R. H. (Dept. Path., U. Texas Med. Branch Galveston). Texas Rep. Biol. Med. 21(1):65-73, 1963.

Intratracheal admin. of urethan (U; 20 ml of 1% aqueous soln., repeated in 2 days) to 35-day-old white Pekin ducks produced foci of granulomatous inflammation in the respiratory tract with irregular, granular, yellowish-brown areas of necrosis containing eosinophilic bodies which were suggestive of mammalian RBC, but no pulmonary tumors appeared. Moreover, U had no significant effect on the incidence or type of pulmonary tumors produced by the intratracheal admin. of 20-methylcholanthrene (20-Me; 20 ml of 0.5% soln. in 1% Tween 80), either 62 days before, simultaneously with, or 60 days after U treatment. A variety of tumors, including lipoma, fibroma, carcinoma, sarcoma, adenocarcinoma, neurofibroma, ganglioneuroma, hemangioma and mixed tumors, as well as necrotic foci and fluid-filled cystic spaces in the mesentery, were found in all groups. Tumor incidence varied from 54.2% in those given

only 20-Me and Tween 80 to 32-34.6% in those created with U at the time of or following admin. of 20-Me, and 16.7% in ducks pretreated with U 50 days before (which were therefore 101 days old at the time of 20-Me inj.). Interesting findings included the appearance of hemangiomas in the legs and feet of some ducks following intratracheal admin. of 20-Me, and in 1 duck a pulmonary sarcoma which apparently metastasized to the myocardium. Degenerative necrosis of the striated musculature and amyloidosis of the liver were also found in all groups and are considered spontaneous.

3-675 INDUCTION OF CANCER IN RATS BY APPLICATION OF DIETHYLNITROSAMINE AND X-IRRADIATION. (Ger.) Schmäh, D. (Inst. Path., Rheinische Friedrich-Wilhelms U., Bonn, Germany), J. Thomas, and E. Stutz. Naturwissenschaften 0(7):308-309, 1963.

One group of Wistar rats of both sexes (I) received diethylnitrosamine (DENA), 3 mg/kg/day, s.o. from the 90th day of life, while a 2nd group (II) received the same treatment \pm whole-body X-irradiation on the 89th day of life. Both groups developed hepatocellular carcinomas which were morphologically identical. The mean effective dose of DENA was 690 ± 53 mg/kg for I with a mean latent period of 230 ± 18 days, while for II mean effective dose was 674 ± 45 mg/kg and mean latent period was 225 ± 15 days. These differences were not considered statistically significant.

3-676 RESEARCHES ON THE ACTION OF PROCAINE, PABA, LIGNOCAINE AND SULFASOMIDINE ON THE GROWTH OF WALKER 256 ADENOCARCINOMA, IN THE RAT. (Rum). Gheorghiu, P. (Med. Pharm. Inst., Bucharest, Rumania), D. Dobrescu and P. Udrea. Stud. Cercet. Fiziol. 8(1):117-123, 1963.

Groups of 10 rats of both sexes, 5 days after transplantation with Walker 256 adenocarcinoma, were inj. with various drugs. Procaine HCl (1% in water, 0.5 ml/day \times 12, i.p.) in 2 experiments led to 156% and 358% increased tumor growth compared to controls; p-aminobenzoic acid (PABA; 5 g% in water, 0.5 ml/day \times 12, i.p.) increased tumor growth by 35% while diethylaminoethanol (0.38 g% in water, 0.5 ml/day \times 12, route not stated) and lignocaine (2% soln., 0.25 ml/day \times 12, i.p.) had no effect. Sulfasomidine ("Elkosil"; 5 soln., 0.5 ml/day \times 12, i.m.) admin. concurrently with procaine HCl (same dose used previously) completely inhibited the stimulatory effect of the procaine. The stimulatory action on tumor growth is attributed to the PABA which results from the hydrolysis of the procaine HCl in the body; lignocaine (also a local anesthetic) does not liberate PABA and hence did not influence tumor growth; sulfasomidine, a PABA-antagonist, inhibited completely the action of procaine.

63-677 VASCULAR MODIFICATIONS DURING EXPERIMENTAL CARCINOGENESIS OF THE CHEEK POUCH OF THE GOLDEN HAMSTER. (Fr., Abstract) Delarue, J., J. Mignot and T. Caulet. Path. Biol. 11(7-8):528, 1963.

In the early phases of carcinogenesis induced in the cheek pouch of golden hamsters by 9,10-dimethyl-1,2-benzanthracene, the veins and capillaries increased in diameter, and the connective tissue stroma showed structural modifications. Formation of papillomatous tumors was accompanied by the appearance of clusters of dilated capillaries, irregular in structure. Eventually epitheliomas appeared, and their vascularization showed a more marked degree of disorganization than was observed surrounding the benign tumors.

63-678 BIOCHEMICAL FACTORS IN THE ETIOLOGY OF CARCINOMA OF THE BLADDER. THE ROLE OF β -GLUCURONIDASE. (E.) Kerr, W. K. (Banting Inst., U. Toronto, Ontario), M. Barkin, J. D'Aloisio and Z. Menczyk. Cancer 16(5):633-638, 1963.

That glomerular filtration is not the only source of urinary- β -glucuronidase (UBG) is evidenced by the lack of correlation between UBG and creatinine levels and the production of glucuronidase in an intact but surgically isolated bladder of a man after instillation through a cystotomy tube of a glucuronidase-free soln.; the isolated bladder secreted UBG to a degree proportional to the specific gravity of the soln. For specific gravities of 1.004, 1.007, 1.030, and 1.033, UBG in units/ml were 2.61, 4.78, 12.78, and 14.16, resp.; pH had little effect. Postoperatively there is a non-specific rise in glucuronidase levels in urine that returns to normal in 14-28 days. Definitive surgical removal of a bladder tumor when the UBG was as high as 24,000 units per 24 hr. resulted in a return of UBG to normal levels; incomplete removal resulted in persistent elevation. UBG was elevated in 2 pts. with hypernephroma, returning to normal with removal and increasing in 1 with tumor recurrence. The UBG elevation may be the result rather than the cause of the tumor.

63-679 DEVELOPMENT OF MALIGNANT LYMPHOMAS BY CELL-FREE FILTRATES PREPARED FROM A CHEMICALLY INDUCED MOUSE LYMPHOMA. (E.) Toth, B. (Div. Oncol., Chicago Med. Sch.). Proc. Soc. Exp. Biol. Med. 112(4):873-875, 1963.

A cell-free filtrate was prepared by the Gross technic from a thymic tumor of a 16-week-old Swiss mouse induced by a single s.c. inj. at birth of 100 μ g of 9,10-dimethyl-1,2-benzanthracene (DMBA) and cytologically diagnosed as malignant lymphoma, stem cell type. After s.c. inj. of 0.05 ml of a 1:5 dilution of the filtrate into newborn (less than 24 hr. old), random bred mice, 7/8 survived, 6 (87.5%) of which developed malign-

nant lymphomas (5 of the lymphocytic type and 1 histiocytic), and 1 died showing evidence of a lymphoid tumor. Mice receiving 0.1 ml i.p. of the filtrate at the age of 8 wk. developed no such tumors. The incidence of malignant lymphoma in 29 female and 28 male untreated controls was 17.4% and 3.5%, resp. Macroscopically the malignant lymphomas were either thymic or generalized. The tumors are not believed to be spontaneous or to be induced by residual DMBA in the tumor from which the filtrate was prepared.

- 63-680 EFFECT OF OESTROGEN ON THE FEMALE GENITAL TRACT AND MAMMARY GLAND OF MICE. Rao, P. S. (Guntur Med. Coll., India) and D. J. Reddy. *J. Indian Med. Assn.* 40(7):321-324, 1963.

After s.c. admin. of 0.1 mg of estradiol benzoate x 1/wk. or x 1 every 5 days in addition to application of smegma to female Swiss albino mice, cervical keratinization (CK) was seen in about 80%, in addition to epithelial hyperplasia (CEH), basal cell hyperplasia (BCH), adenomatous hyperplasia (CA), chronic cervicitis (CC) and glandular epidermidalization (CGE). In the uterus, endometrial hyperplasia (UEH) and cystic dilatation (UCD) of the glands was seen in 33.3 and 28.6%, resp., along with glandular epidermidalization, cystoglandular hyperplasia (UCG) and myometrial hyalinization (UM). Adenocarcinoma, and follicular cysts of the ovary and breast adenocarcinoma occurred in 4.8%, 14.3% and 4.8%, resp. In normal virgin mice, CEH, CC, and CGE, occurred in 37.5%, 37.5% and 75%, resp.; in the uterus, UEH, UCD, and adenomyosis occurred in 37.5%, 37.5%, and 25%, resp. In 5 parous breeders CC and CGE was found in all mice; CC was also found in 2/2 sterile breeders. It is suggested that the hyperplastic and metaplastic changes seen in virgin mice might be due to endogenous estrogen excess.

- 63-681 CARCINOGENIC EFFECTS OF ADSORBATES OF RAW AND FINISHED WATER SUPPLIES. (E.) Hueper, W. C. (NCI, Bethesda, Md.) and W. W. Payne. *Am. J. Clin. Path.* 39(5):475-481, 1963.

Raw water studied was from a river downstream from chemical and rubber plants; approx. 170 gallons yielded 1 g of chloroform extract and approx. 1150 gallons yielded 1 g of an ethanol extract. In terms of finished water (from a town's drinking water), for similar quantities of chloroform and ethanol extracts, 620 and 890 gallons, resp., were needed. After inj. of chloroform eluates which contained the aromatic fraction of hydrocarbons from adsorbates of raw water (2 mg in 0.05 ml tricapylin per 2 wk. x 28, s.c.) into C57 mice, of 4/72 tumors which developed at the site of inj., 3 were spindle cell sarcomas; one developed a papilloma of the bladder. After cutaneous admin. of 1 drop of this extract every 2 wk. x 28, 1/72 developed a reticulum cell sarcoma of the liver and another

developed leukemia or lymphoma. When chloroform extracts of finished water (4 mg in 0.05 ml tricapylin, s.c.) were admin. 2/72 developed lymphoma or leukemia; no tumors developed from cutaneous admin. After cutaneous and s.c. (4 mg in alcohol every 2 wk. x 20) of ethanol extracts (detergent and phenolic constituents) of raw water and s.c. admin. of finished water each led to 1 case of lymphoma or leukemia. Some of the mice painted with the alcohol extract exhibited chronic epidermal ulcers revealing hyperplastic epidermis in the marginal sections. Cutaneous admin. of alcohol extracts of finished water or oral admin. of chloroform extracts did not produce tumors. The bladder papilloma points to probable contamination of the water from rubber manufacturing plants.

- 63-682 OCULAR ANOMALIES IN ASSOCIATION WITH DEVELOPMENTAL LIMB ABNORMALITIES OF DRUG ORIGIN. (E.) Gilkes, M. J. (Chailey Heritage, Craft Sch. Hosp., Sussex, England) and M. Strode. *Lancet* 1:1026-1027, 1963.

Ocular changes in 7/20 cases of developmental anomalies at Chailey Heritage, which are probably associated with maternal thalidomide admin., include the whole range of abnormality associated with the various stages of failure of closure of the fetal fissure of the embryonic eye. The eye lesions appear to bear no specific relation to the type of limb deformity. In a series of 7 cases of limb agenesis or deformity arising before the advent of thalidomide, there were no eye changes.

- 63-683 THE INDUCTION AND ULTRASTRUCTURAL STUDY OF AMELANOTIC DERMAL MELANOCYTOMA IN THE SYRIAN ALBINO HAMSTER. (E.) Nakai, T. (Chicago Med. Sch., Chicago, Ill.). *Lab. Invest.* 12(5):554-562, 1963.

After application of a single dose of 800 µg of 9,10-dimethyl-1,2-benzanthracene (DMBA; 1% in mineral oil) to the dorsal skin of Syrian albino hamsters, 7/10 developed amelanocytic tumors resembling neurofibromas of man in 14-31 wk. Except for absence of melanin the tumors were morphologically identical to those induced in golden and white hamsters. The av. number of tumors per tumor-bearing animal was 2.5. Numerous PAS-positive, Feulgen-negative oval or needle-shaped granules believed to contain a protein-carbohydrate complex were found in tumor cells but not in the normal skin of ears, perineum or in the retina. Electron microscopic observations of these tumors revealed bizarre pigment granules which varied in size, shape, and internal structures. The fine structure of the granules in the tumors of the albino hamster were identical to those of melanotic tumors of white hamsters except for the absence of melanin. The capacity of the melanocytes to form melanin after exposure to DMBA is not essential for the melanocytic tumor-

Inducing effect of this carcinogen. The large granules are believed to be the final stage of evolution; the presence of melanin may be required for further development.

63-684 OCCURENCE OF HEPATOMAS IN RATS FED DIETS CONTAINING PEANUT MEAL AS A MAJOR SOURCE OF PROTEIN. (E.) Salmon, W. D. (Dept. Animal Sci., Agric. Exp. Sta., Auburn U., Alabama) and P. M. Newberne. Cancer Res. 23(4):571-575, 1963.

Hepatomas developed in 64/73, and kidney tubule adenomas in 16/73 Charles River C D strain rats fed diets containing 33.3% commercial peanut meal, 7.9% dried lean beef or commercial casein, and 20% fat. When the peanut meal was extracted for 72 hr. with hot methanol, only 15/88 rats developed hepatomas, and none developed kidney adenomas. When the peanut meal was withdrawn from the diet entirely without reducing the total level of dietary protein of 50 rats, no tumors of any kind developed. These results suggested the presence of a carcinogenic agent in the commercial peanut meal (which could be substantially decreased by extraction with methanol). Hepatoma incidence was not decreased by further supplementation of the tumor-inducing diet with choline chloride or DL-methionine. The possibility that the commercial peanut meal used in these experiments contained some toxin-producing fungus could not be ruled out.

63-685 HEPATOMAS IN RATS FED DIETS CONTAINING COMMERCIAL PEANUT MEAL. (E., Abstract) Salmon, W. D. (Dept. Animal Sci., Agric. Exp. Sta., Auburn U., Alabama), P. M. Newberne and C. D. Prickett. Fed. Proc. 22(2):262, 1963.

In a previous report 64/73 Charles River CD strain rats fed a diet containing peanut meal + dried lean beef or casein developed hepatomas (see CRA 1(4):#684, 1963). In the present study, hepatomas developed in 98/113 rats fed a diet containing peanut meal as the sole source of protein, or supplemented with dried lean beef or commercial casein. The tumors developed throughout the livers as multiple nodules a few mm. to several cm. in size. In some cases there was invasion of the mesentery and diaphragm, and metastases to the lungs. There was also a variable degree of bile duct proliferation; cirrhosis was minimal or absent. No hepatoma occurred in 50 rats fed similar diets containing dried lean beef, in 10 fed commercial casein or in 10 fed commercial casein and commercial soy bean as the sole sources of protein.

63-686 HEPATIC CHANGES IN DUCKLINGS AFTER FEEDING CERTAIN PEANUT MEALS. (E., Abstract) Newberne, P. M. (Dept. Nutrition and Food Sci., MIT, Cambridge, Mass.) and W. W. Carlton. Fed. Proc. 22(2):262, 1963.

At the end of 30 days 60-100% of ducklings fed several samples of peanut meal (from peanuts grown in the U. S. and obtained from different processors) developed bile duct proliferation and nodular hyperplasia of the liver. These changes were seen in animals fed a sample of peanut meal found to be carcinogenic to rats (see CRA 1(4):#684 and #685, 1963), or one of 4 other meals. Each peanut meal supplied 75% of the dietary protein. There was no correlation between body wt. response and the liver changes.

63-687 CARCINOGENESIS AND TUMOR INHIBITION BY TRANS N-HYDROXY-4-ACETYLAMINOSTILBENE. (E., Abstract) Andersen, R. A. (U. Wisconsin, Madison), M. Enomoto, J. A. Miller and E. C. Miller. Proc. Am. Assn. Cancer Res. 4(1):2, 1963.

N-hydroxy-4-acetylaminostilbene (N-HO-AAS), a suspected intermediate in the metabolism of 4-aminostilbene (AS) and of 4-acetylaminostilbene (AAS), was more carcinogenic than either of the parent compounds and was also a stronger inhibitor of the Walker 256 tumor. In weanling rats 2% of the admin. AS was recovered as N-HO-AAS. After inj. of AAS (5.3 μ moles/wk. x 5, s.c.) to female rats, 1 of 17 rats had 3 mammary carcinomas by 9 mo. Of 17 rats given N-HO-AAS, 11 had a total of 14 mammary carcinomas, and 2 had sarcomas at the inj. site. In a second experiment the total numbers of mammary carcinoma at 25 wk. were N-HO-AAS 23/20, AAS 10/20, and AS 12/20. When N-HO-AAS was inj. i.p. (0.71 μ moles/100 g 3 x/wk. x 11), 10/23 female rats had 13 mammary tumors at 28 wk., while only 1 given AAS had a tumor. When N-HO-AAS (0.21 μ moles/kg in the diet for 18 wk.) was fed to male rats, 10/17 had ear duct carcinomas, 2 adenocarcinoma of the small intestine, 2 liver carcinomas, and 8 multiple papillomas of the forestomach by 9 mo. Of 17 rats fed AAS, 9 developed ear duct carcinomas.

63-688 A SHORT TERM TEST FOR CARCINOGENICITY. MOUSE EMBRYO TISSUE HOMOGRAFTS IN BALB/c STRAIN MICE. (E.) Peacock, P. M. (Royal Beatson Mem. Hosp., Glasgow, England) and E. Dick. Brit. J. Cancer 17(1):59-61, 1962.

See CRA 1(3):#414, 1963.

63-689 INDUCTION OF HEPATOMAS BY THIOURACIL IN INBRED STRAINS OF MICE. (E.) Casas, C. B. (U. Puerto Rico Med. Sch., San Juan). Proc. Soc. Exp. Biol. Med. 113(2):493, 1963.

Admin. of a diet containing 0.3% thiouracil (TU) for 18 mo. to a subline of C3H mice produced hepatomas in 87% (14/16) of the females and 92% (12/13) of the males compared with controls: 0% in 24 females and 6.6% (2/32) in males. Hepatomas found in TU-fed mice appeared identical to those found in controls. When inbred TM mice were used, no hepatomas were observed in 44 TU-

fed mice and 40 controls. The author suggests that genetic susceptibility must be present for development of hepatomas and for their increased incidence in mice treated with TU.

- 63-690 ESOPHAGEAL TUMORS PRODUCED IN RATS BY THE FEEDING OF DIHYDROSAFROLE. (E., Abstract) Long, E. L. (Div. Pharmacol., Food Drug Admin., Washington, D. C.) and P. M. Jenner. Fed. Proc. 22(2):275, 1963.

Primary esophageal tumors, generally involving half or more of the length of the organ, were induced in 75% Osborne-Mendel rats receiving 10,000 or 5000 ppm of the flavor dihydrosafrole in their diet for 2 yr. The tumor incidence dropped to 20 and 0% in rats receiving 2500 and 1000 ppm, resp. Approx. 2/3 of the tumor bearing rats at the 10,000 ppm level, and 2/5 at the 5000 ppm level had papillary epidermoid carcinomas, while the remaining tumors were classified as benign epidermoid papillomas. In contrast to safrole, dihydrosafrole did not induce liver tumors in significant numbers. In rats, the carcinogenic effect of dihydrosafrole resembles, in terms of the target organ that of certain nitroso compounds.

- 63-691 STUDIES ON THE MICROSOMAL N-HYDROXYLATION OF 2-ACETYLAMINOFLUORENE. (E., Abstract) Irving, C. C. (VA Hosp., U. Tenn. Med. Units, Memphis). Fed. Proc. 22(2):296, 1963.

The formation of N-hydroxy-acetylaminofluorene (N-OH-AAF) from AAF by rabbit liver microsomes (in the presence of NADP and oxygen) was assayed with added sodium fluoride (0.1 mmole/ml) to prevent further metabolism of N-OH-AAF. Using this assay, formation of N-OH-AAF was shown to occur in the liver microsomes of hamsters, dogs and cats, but not of rats, mice or guinea pigs.

- 63-692 PHOTODYNAMIC ACTIVITY OF POLYCYCLIC COMPOUNDS. (E., Abstract) Small, M. (Child. Cancer Res. Foundation and Harvard Med. Sch., Boston, Mass.) and S. S. Epstein. Fed. Proc. 22(2):316, 1963.

The photodynamic activities of low concentrations of 150 polycyclic compounds were compared on the basis of time required to immobilize *Paramecium caudatum* exposed to long wave UV irradiation. Photodynamic activity of varying degree was observed among tetracyclic, pentacyclic, and hexacyclic compounds, including many established carcinogenic agents. The system has been investigated as a possible short term test for potential polycyclic carcinogens. (See also CRA 1(2):#192, 1963.)

- 63-693 THE EFFECT OF LOCAL TISSUE INJURY ON THE INCIDENCE OF GLIOMAS IN RATS INGESTING 2-AAF. (E., Abstract) Battifora, H. (Presbyterian-St. Luke's Hosp., Chicago, Ill.), R. A. Glasen and R. Oyasu. Fed. Proc. 22(2):317, 1963.

In Wistar rats fed 2-acetylaminofluorene there were 5 gliomas among 202 brains examined (3 astrocytomas and 2 ependymomas, 4 in the cerebral hemispheres and 1 in the cerebellum). There was no significant difference between this tumor incidence and the incidence of gliomas in 104 untreated controls. Damaging the cerebral cortex by application of solid carbon dioxide, followed by the carcinogenic diet resulted in 1 subcortical astrocytoma among 25 experimental animals which, again, was not significant.

- 63-694 ANNULMENT OF 4-NITROQUINOLINE N-OXIDE TOXICITY IN TISSUE CULTURE SYSTEMS. (E., Abstract) Amsterdam, D. (Jewish Chronic Dis. Hosp., Brooklyn, N. Y.) and A. C. Zahalsky. Fed. Proc. 22(2):373, 1963.

The cytotoxicity of 4-nitroquinoline-N-oxide (4-NQ, $4 \times 10^{-6}N$) to HAD and HeLa cells in test tube cultures was prevented by L-tryptophan (20 mg%), nicotinic acid (2 mg%), phthiocol (0.2 mg%) and liver "L" (20 mg%) singly or in combination. These aromatic metabolites were also found to prevent 4-NQ toxicity in protozoan cultures (*Ochromonas danica* and *Euglena gracilis*). The data suggest that these aromatic metabolites overcome the block(s) induced by 4-NQ interference with NAD precursors.

- 63-695 SOLUBLE PROTEINS OF LIVER NUCLEI IN AZO HEPATOCARCINOGENESIS. (E., Abstract) Bakay, B. (Inst. Cancer Res., Philadelphia, Pa.), R. S. Ho and S. Sorof. Fed. Proc. 22(2):477, 1963.

Saline-phosphate soluble nuclear proteins from rat liver nuclei and 3'-methyl-4-dimethylaminoazobenzene-induced rat liver tumor nuclei contained 42-50% and 38-40% of the nuclear nitrogen, resp. Boundary electrophoresis of liver nuclear proteins at pH 8.6 showed 1 basic and 8 acidic protein classes, whose relative amounts were unchanged in liver nuclei from rats fed the carcinogen for 2.5 wk. The carcinogen-induced tumors showed no basic component and, of the 9 acid components present, there was a decrease in the amount of near-neutral proteins, and an increase of the more acidic proteins. Analytical ultracentrifugation has shown that the soluble nuclear protein of various livers contain 3 rapidly sedimenting and 4 larger slower components, whose amounts change during preneoplasia. In contrast, the liver tumor nuclei show only 2 fast and 2 large slowly sedimenting components.

63-696 DIBENZANTHRACENE FIBROSARCOMA INDUCTION IN SEVERAL PIGEON BREEDS. (E., Abstract) Eubanks, J. W. (Bowman Gray Sch. Med., Winston-Salem, N. C.), C. C. Hazlett and R. W. Prichard. Fed. Proc. 22(2):315, 1963.

1,2,5,6-Dibenzanthracene (0.1 ml 3% benzol suspension) in each pectoral muscle produced fibrosarcomas within 6 1/2 mo. in 0/24 White Carneau, 1/23 Show Racers, 1/21 Racing Homers and 3/27 Domestic Flight pigeons, all inoc. at 1-2 yr. and surviving 5 mo.; and in 6/8 Domestic Flights and 3/6 Show Flights inoc. at 5-6 yr. and surviving over 5 mo. The older Flights came from a different source than the younger pigeons, and strain differences may account for the significant increase in tumor susceptibility.

63-697 SOLID STATE CARCINOGENESIS. (E., Abstract) Bischoff, F. (Cottage Hosp. Res. Inst., Santa Barbara, Calif.) and G. Bryson. Fed. Proc. 22(2):315, 1963.

Comparison of s.c. implants into ovariectomized female Marsh mice aged 4 mo. of mats of air dried cholesterol crystals (20 mg/mouse) and cholesterol powder (same amounts, particle size 2-4 x the diameter of a RBC) caused cysts with walls of young connective tissue in 3% and 37%, resp.; small spaces about granulomatous tissue in 18% and 18%, resp., and larger acicular spaces with more collagen and a few giant cells in 64% and 0%, resp. The high incidence of noninflammatory reaction from the crystal series parallels results obtained for plastic films vs. powders. Inj. s.c. of super- and undersaturated solutions of cholesterol in olive oil (20 mg/mouse) and inj. of a vehicle control produced reactive cystic fibrosis in 82%, 42% and 15% of mice, resp. Two local sarcomas were found in the super-saturated series, 1 surrounding crystals.

63-698 MOUSE LEUKEMIA RESULTING FROM THE IMPLANTATION OF AN ACTH-SECRETING PITUITARY TUMOR. (E., Abstract) Handler, A. H. (Child. Hosp. Med. Center, Boston, Mass.) and C. Wills. Fed. Proc. 22(2):605, 1963.

In the 9th l.m. passage of an ACTH-secreting pituitary tumor, AtT 18VC-Furth, in intact mice, the tumor transplants regressed in all 7 recipients. Two mo. later, 1 of the 7 recipients developed a lymphocytic leukemia which has been transferred through 9 passages i.v., s.c. or i.p. in 361 LAF1 mice. This leukemia did not grow in 15 C57Bl/6, 10 AKR, 10 ALF1 or 10 Swiss mice, and could not be transmitted with 2 ultrafiltrates in 59 LAF1 mice. Other leukemias have developed subsequently in LAF1 mice that have regressed the pituitary tumor, but to date none is transplantable.

63-699 EFFECT OF DIETHYLSTILBESTROL AND EXTERNAL RADIATION ON PROPYLTHIOURACIL-INDUCED THYROID HYPERPLASIA IN THE MALE SYRIAN HAMSTER. (E., Abstract) Dekker, A. (Child. Cancer Res. Foundation and Harvard Med. Sch., Boston, Mass.) and A. B. Russfield. Fed. Proc. 22(2):563, 1963.

Male Syrian hamsters maintained on laboratory chow + propylthiouracil (PTU; 0.1% in drinking water x 12 mo.) showed a 2-3 x increase in thyroid wt. Animals on the same regimen + diethylstilbestrol (DES; 15 mg s.c.) or irradiated (100 r whole body) at the beginning of the experiment showed a 10-15 x increase in thyroid wt. Neither X-rays nor DES alone had any effect on thyroid wt., and animals given PTU + DES + X-rays showed no further increase in thyroid wt. DES induced pituitary and hypothalamic changes, but there was no correlation between pituitary and thyroid wt.

See also abstract nos.: 593,596,597,600,610, 613,621,755,763

VIRAL CARCINOGENESIS

- 63-700 EXPERIMENTAL RESEARCH ON THE MECHANISM OF CARCINO- AND LEUKEMOGENESIS FROM THE VIEWPOINT OF CELL-GENETICS AND VIRUS. (Jap.) Awano, I. (1st. Dept. Int. Med., Fukushima Med. Coll., Japan), S. Toshima, F. Tsuda, H. Sato, R. Fukuda, K. Abe, K. Kokubun, S. Matsuyama, T. Hashimoto and I. Takahashi. Nippon Naika Gakkai Zasshi (J. Jap. Soc. Intern. Med.) 51(5): 569-578, 1962.

In 8 kinds of spontaneous mouse leukemia (7, AKR and 1, C58) and 5 spontaneous mouse mammary carcinomas (1, C58; 3, C3H and 1, dd) virus was always found in the tumor tissue, mainly in the intercellular space. There was little variation from somatic cells as regards the chromosome picture. The cell free organ extract from 3 of the spontaneous AKR leukemias, when injected into other mice induced leukemia, the cells of which showed almost the same chromosome picture as in the original tumor; however, 1.5 to 6 mo. later the chromosome picture, in most instances, was considerably altered. While virus content of tumor tissue tended to decrease with each successive transplantation, there was little change in the karyotypes. It was concluded that the virus must be related to the induction of mouse leukemia and mammary cancer, but not to tumor reproduction.

- 63-701 EXPERIMENTAL INVESTIGATIONS IN MURINE AKM LEUKEMIA. (E.) Nastac, E. (Inst. Inframicrobiol. R. P. R. Acad., Bucarest), B. Anagnoste and G. Balmus. Neoplasma (Bratisl.) 10(1):51-59, 1963.

In guinea pigs and rabbits intracerebral inoc. of a suspension of AKM leukemia tumor, its cell free filtrate, or of total leukemic blood produced an encephalopathy which was serially transmissible. These same products, inoc. into white hybrid mice, produced encephalopathy but also caused the appearance of tumors histopathologically similar to one another and to the original tumor of the leukemic mouse. Intracerebral passage of the pathologic material in heterologous species (guinea pig, rabbit) followed by renewed inoc. into the homologous species (mouse) resulted in exacerbation of the virulence of the pathogenic factor, manifested by a systemic disease transmissible to this species up to the seventh passage. In this case this was associated with the appearance of a tumor similar to the original AKM tumor.

- 63-702 METABOLISM OF VIRUS INDUCED LEUKEMIC LEUKOCYTES. REPORT I. GLYCOLYSIS IN INTACT CELLS IN RINGER SOLUTION AND SERUM. (Ger.) Bielka, H. (Inst. Exptl. Cancer Res., German Acad. of Sci., Berlin-Buch) and I. Schneiders. Zschr. Krebsforsch. 65(3):173-181, 1963.

Aerobic glycolysis in serum is significantly lower in the leukocytes of rats or mice with lymphatic

AKR leukemia ($2.05 \text{ mm}^3 \text{ CO}_2/\text{hr./cell} \times 10^{-7}$) and white myeloid leukemia (2.38) than in bone marrow cells (4.65); in cells of myeloid chloroleukemia, it is 9.65 and in cells of transplantable myeloid leukemia (SOV 16), 24.3. There is a positive correlation between the degree of ploidy of the cells and the extent of glycolysis. Anaerobic glycolysis was, resp., 13.85, 11.1, 12.2, 41.2 and $61.5 \text{ mm}^3 \text{ CO}_2/\text{hr./cell} \times 10^{-7}$, showing tumor-like high values for cells of the transplantable myeloid leukemia. In comparison to bone marrow cells, the virus-induced leukemic cells show different values when calculated to dry wt. of cells, DNA content or per cell; these values depend on the degree of maturity of the leukemic cells.

- 63-703 METABOLISM OF VIRUS INDUCED LEUKEMIC LEUKOCYTES. REPORT II. GLYCOLYSIS IN HOMOGENATES. (Ger.) Bielka, H. (Inst. Exptl. Cancer Res., German Acad. Sci., Berlin-Buch) and L. Venker. Zschr. Krebsforsch. 65(3):182-186, 1963.

The effective glycolysis, i.e., glycolysis of intact cells, was $4.6 \text{ (Q}_{\text{lactic acid}}^{\text{O}_2})$ and the glycolytic capacity, i.e. of the homogenate, was 62 for virus-induced myeloid leukemia; 5.4 and 56, resp., for virus-induced lymphatic leukemia; and 25.1 and 68, resp., for transplantable myeloid leukemia (SOV 16). The inhibitory factors present in the WBC of virus-induced leukemias are removed during cellular transplantations of the disease, with an increase of the effective glycolysis to that typical of tumor cells.

- 63-704 METABOLISM OF VIRUS-INDUCED LEUKEMIC LEUKOCYTES. REPORT IV. CRABTREE-EFFECT. (Ger.) Bielka, H. (Inst. Exptl. Cancer Res., German Acad. Sci., Berlin-Buch). Zschr. Krebsforsch. 65(3):196-200, 1963.

In intact cells of lymph nodes and thymus of mice with virus-induced myeloid leukemia in which the aerobic glycolysis is slight ($\text{Q}_{\text{lactic acid}}^{\text{O}_2} = 4.55$) the addition of glucose to the medium causes a 19% decrease in oxygen consumption in Krebs-Ringer solution without phosphate; in the strongly glycolyzing cells of transplantable myeloid leukemia SOV 16 ($\text{Q}_{\text{LA}}^{\text{O}_2} = 18.4$), a 52% decrease was observed under the same conditions; in cells of virus-induced lymphatic AKR-leukemia, there was an increase in oxygen consumption of 66%. In the presence of 15 mM inorganic phosphate, the action of glucose on metabolism is less varied, decreasing the oxygen consumption -3.8% and -22%, resp., for the first two and having no effect on cells of the third type of leukemia.

- 63-705 INHIBITORS OF POLYOMA VIRUS HEMAGGLUTINATION IN SERA AND ORGANS OF NORMAL MICE. (It.) Balduzzi, P. (Inst. Microbiol.,

J. Florence) and S. Salmon. Sperimentale 112(6):446-456, 1962.

Organ extracts and sera from 160 normal and 20 immune mice contained polyoma virus hemagglutination inhibiting activity. Heating at 37°C for 15 minutes decreased this inhibitory activity showing that the virus nonspecific-inhibitor bond is thermolabile, and therefore not due to antibodies. No difference could be observed in the inhibition induced by organ extracts from immune and from normal mice, but a comparison between this activity and that of normal sera suggests different binding properties at 4° and at 37°C. Organ extract inhibitors bind the virus at 4°C and at 37°C, but less efficiently at the higher temperature. Serum inhibitors were demonstrable only at 4°C. Lung, salivary, and brain extracts showed higher activity than kidney, thymus, liver, and brown fat extracts.

63-706 IMMUNOLOGICAL TOLERANCE, INFECTIVE TOLERANCE AND VIRUS-INDUCED NEOPLASTIC TRANSFORMATION. (E.) Stansly, P. G. (Dept. Microbiol., Wayne State U., Detroit). Nature (London) 198:110-111, 1963.

The term "immunological tolerance" has been used to describe the condition where antigens fail to induce antibody production in the adult animal as a result of previous experience with the specific antigen pre- or post-natally. Infective tolerance, on the other hand, appears to be a function of the particular target cells involved in the disease which, by some undefined mechanism become resistant to the destructive action of the virus. Rubin has observed that chickens congenitally infected with lymphomatosis virus (and both infectively and immunologically tolerant), nevertheless, succumb to the neoplastic disease, and in much greater numbers than chickens which are not tolerant. This result would appear unexpected in terms of what occurs in mice congenitally infected with the virus of lymphocytic choriomeningitis and which develop a viremia without antibody formation (immunologic tolerance) and hence are unaffected by the subsequent intracerebral inoc. of the virus (infective tolerance). The high incidence of chicks dying of lymphomatosis appears to indicate that in tumor viruses the cytopathogenic, but not the neoplastic activity is abolished by infective tolerance. Dulbecco has concluded that the transforming activity of polyoma virus is a property unrelated to more conventional characteristics, such as persistence in cells and cytopathogenic activity.

63-707 ATTEMPTS TO RE-ISOLATE POLYOMA-VIRUS STRAIN BB/T2 FROM TUMORS OF RATS, GOLDEN-HAMSTERS, MICE, AND RABBITS. (Ger.) Raffi, A. (Inst. Med. Biol., Ger. Acad. Sci., Berlin), J. Gimny and W. Krischke. Arch. Geschwulstforsch. 20(2):103-124, 1963.

A total of 42, non-homogeneous, BB/T2-induced tumors (mostly sarcoma) from 4 different animal species (27 from rats, 7 from golden hamsters, 6 from mice, and 2 from rabbits) was used in virus re-isolation experiments in vivo (76 trials). Active, cell free G-4 filtrates were found in 19% of all tumors (approx. 30% hamster, 50% mice, but none from rabbits). Filtrates from various tumors (0.1-0.8 ml, s.c.) were inj. into groups of 296 newborn rats, 65 hamsters and 550 mice. In the rat, 1 uterine sarcoma and 3 fibrosarcomas were induced in 769 and 91-159 days, resp.; 1 osseous sarcoma and 1 fibroma were induced within 327 and 219 days, resp., total, 2%. In the hamster, 1 fibroma and 1 fibrosarcoma were induced within 120 and 97 days, resp.; 1 lipoma was induced within 365 days: total 4.6%. In the mouse, 2 parotid tumors and 2 uterine and 1 polymorphocellular sarcomas were induced within 580-806 days; and 1 parotid tumor was induced in 262 days by a filtrate of a mouse parotid tumor: total 1.1%. When added to mouse embryo tissue cultures, a cytopathogenic effect (CPE) was seen with tumor suspension from 1 of the original hamster tumors, 50% of those from rats, 66% from rabbits and all of those from guinea pig or mouse tumors. Passage through as many as 40 tumor generations revealed decreasing CPE, and no virus was detected after the 21st passage. In vitro virus re-isolation was 100% successful for malignant parotid tumors of mice. In rats, better isolation results were seen in the benign =90% than in malignant tumors. The oncogenic activity, in vivo and in vitro, of tumor-culture suspensions derived from animals inoc. with re-isolated virus was also studied by the same methods. Most active, in vivo and in vitro were cell suspensions of mouse tumors, followed by those of rabbit, rat, and hamster tumors. Most susceptible to both homologous and heterologous inoc. was the rat; then the mouse; least susceptible was the golden hamster.

63-708 ULTRAMICROSCOPIC FINDINGS OF VIRUS-LIKE APPEARANCE IN CARCINOMA OF THE PORTIO VAGINALIS. (It.) Motta, G. (Obstet. Gynec. Clin., U. Messina, Italy), C. Pullè and V. Capria. Arch. Ostet. Gynec. 67(6):697-714, 1962.

Of 8 cases of carcinoma of the portio vaginalis (3 spinocellular, 5 basocellular) examined by electron microscopy, 3/4 removed at clinical Stage I contained 2 types of abnormal submicroscopic particles located in cytoplasmic vacuoles. The first type consisted of fairly regular aggregates of ovoid masses, 100 mμ in the largest diameter and was apparently covered by a thin membrane. In some malignant cells from 2/3 cases there were smaller particles about 40-50 mμ in diameter, spherical in shape, denser and apparently more homogeneous than the first type. Such particles have not been observed in many studies of normal or pathologic (but not neoplastic) epithelium of the portio vaginalis and endocervix.

- 63-709 PRESENCE OF VIRUS-LIKE PARTICLES IN THE TRANSPLANTABLE THYMOMAS OF DBA/2 MICE. ULTRAMICROSCOPIC STUDY OF THEIR FORMATION. (Fr.) Haguenau, F. and K.-H. Hollmann. *C. R. Acad. Sci. (Paris)* 236(16):3541-3544, 1963.

Electron microscopy of a transplantable lymphoblastic lymphosarcoma originally found in the DBA/2 He strain (maintained in solid or ascitic form), showed two types of submicroscopic particles. The first type were found in 10% of cells and consisted of type A intracytoplasmic aggregates near the golgi apparatus. They measured about 70 m μ and were delimited by 2 peripheral membranes with high affinity for uranyl acetate and lead. The center had low electron density and did not contain a nucleoid. However, in all tumor cells there was also a second previously unreported type of particle with a double membrane measuring 70 m μ . The inner portion of the membrane showed high affinity for uranyl salts and lead. This particle resembled the type A particle in all respects except for its location, which was always in protruded portions of the endoplasmic reticulum. In cells of this tumor, the endoplasmic reticulum was abnormally thickened and exhibited increased affinity for uranyl salts and for lead.

- 63-710 INACTIVATION OF VACUOLATING VIRUS (SV40) BY BETAPRONE. II. EVALUATION OF THE ONCOGENIC PROPERTIES OF SV40 IN HAMSTERS AFTER INACTIVATION WITH BETAPRONE. Hayashi, H. (Henry Ford Hosp., Detroit) and G. A. LoGrippo. *Henry Ford Hosp. Med. Bull.* 11(1):93-97, 1963.

Rhesus monkey kidney extracts containing SV40 were treated with β -propiolactone (Betaprone, BPL; 0.35%) combined with UV. The material, evaluated in 91 suckling hamsters, showed 100% destruction of the oncogenic properties of the SV40 virus. Tissue from primary tumors induced by SV40 was treated with BPL and transplanted into 66 suckling and 5 adult hamsters. None of these animals developed tumors, while all control animals inoculated with non-treated tissue developed tumors.

- 63-711 CHARACTERISTICS OF A HAMSTER CELL CLONE TRANSFORMED BY POLYOMA VIRUS. (E.) Macpherson, I. (Inst. Virol., U. Glasgow, Scotland). *J. Nat. Cancer Inst.* 30(4):795-815, 1963.

A cloned line of Syrian hamster kidney cells (C13) was infected with polyoma virus and a clone, C13-TC6, was prepared from one of the resulting transformed cells. A comparison between the transformed clone and uninfected C13 cells revealed the following new characteristics: a higher plating efficiency; a higher production of nonvolatile acid in culture; ability to initiate tumors in hamsters when 10^6 or more cells were inoc. s.c.; and a tendency to accumulate

chromosome abnormalities and tetraploid cells, though these abnormalities were not immediately associated with transformation. Both the C13-TC6 line and the uninfected control line C13 produce tumors when inj. into the cheek pouch of the hamster.

- 63-712 ENHANCEMENT OF HOST RESPONSE TO SUBLIMINAL DOSES OF ROUS SARCOMA VIRUS BY FREUND'S ADJUVANT. (E.) Rauscher, F. J. (NCI, Bethesda), M. A. Fink and J. P. Kvedar. *J. Nat. Cancer Inst.* 30(4):649-659, 1963.

Rous sarcoma virus (RSV; 0.01 ED50, i.v. or intra-granulomatous) into chicks treated s.c. with complete Freund's adjuvant 15 days previously caused accelerated growth of the granulomas caused by Freund's adjuvant and also invasion of the adjacent muscle. Approximately 15% of these growths yielded 2-3 log pock-forming units of RSV/ml of tissue. The same dose of virus failed to induce tumors in non-adjuvant treated controls and extracts of tissues from control birds were uninfected. The incidence and severity of visceral metastases at higher dose levels were also increased in infected birds previously inoc. with complete adjuvant. Conversely, when chicks were inoc. with a dilution of virus below the ED50 which failed to produce tumors, and were subsequently inoc. with adjuvant, 85% developed significant levels of anti-RSV antibody, although active virus could not be recovered. Control chicks receiving virus, but saline instead of adjuvant, failed to develop measurable amounts of antibody. The amount of antibody produced after inoc. of adjuvant was directly related to the original infective dose of virus. The method allows detection of host response to virus quantities 4-6 log dilutions less than required to induce tumors.

- 63-713 DENSITY GRADIENT ELECTROPHORESIS STUDIES ON HEMAGGLUTINATION PLAQUE FORMATION AND TUMOR INDUCTION OF SE POLYOMA VIRUS. (E.) Cramer, R. (Pasteur Lab. Radium Inst., Paris), E. Stewart and T. E. O'Connor. *Proc. Soc. Exp. Biol. Med.* 112(4):969-973, 1963.

When the supernatant of a 3-day-old secondary mouse embryo tissue culture infected with SE polyoma virus, strain 11189 (SEP) was submitted to electrophoresis in a sucrose density gradient for 2-3 hr. in a pH 8.6 Veronal buffer, a maximum of hemagglutination (determined by the pattern method), tumor induction (by s.c. inj. into newborn hamsters of 0.3 ml of a 1/50 dilution) and plaque forming activity (determined by the endpoint method) were found in the same fraction. Fraction 10 was the only one which all animals responded to with tumors, which developed within 1-2 mo; fractions 7, 11, 12, 14, 15, 16 and 22 also produced 1 or more tumors. It is concluded that the 3 biological activities of SEP can be correlated with particles of the same electrophoretic mobility.

-714 TUMORS INDUCED IN HAMSTERS BY SIMIAN VIRUS 40: PERSISTENT SUBVIRAL INFECTION. (E.) Gerber, P. (NIH, Bethesda, Md.). *Science* 140:889-980, 1963.

EP cells of 2 hamster ependymomas (EP_A, EP_H) induced by intracerebral inoc. with simian virus (SV40) were cultivated *in vitro* for 55 and 56 passages for 14 mo., SV40 was not detected in all free fluids and cell lysates tested on African green monkey kidney cells (GMK) and viral antigen could be detected by the fluorescent antibody technique. All cells retained their neoplastic potential when newborn hamsters were inoc. When EP cells were placed in contact with sensitive indicator cells from GMK, characteristic cytopathogenic effects appeared in 18-20 days in cells adjacent to colonies of EP cells; the virus was identified as SV40. Rabbit kidney cells (RK) infected with SV40 (0.5 TCID₅₀ per cell) failed to support viral growth, whereas exposure of the cells to infectious viral DNA resulted in synthesis of small amounts of virus. Significant amounts of SV40 were recovered from GMK and GMK seeded with 2 x 10⁷ EP_A or EP_H cells: virus was detectable in uninoculated controls when EP cell lysates were inoc. No activity comparable to interferon in EP culture fluids was found. Prolonged passage of EP cells in the presence of high-titer SV40 antiserum did not prevent the infection. EP cells were resistant to reinfection with SV40. It is believed that viral nucleic acid is permanently present in some tumor cells which can introduce the genetic information to indicator cells and thereby initiate viral synthesis. Tumor cells themselves are unable to synthesize infectious virus.

-715 CONTAMINATION OF ADENOVIRUS STOCKS WITH SV40 (PAPOVAVIRUS GROUP). (E.) Chau-Siung Yang (Dept. Virol. Epidem., Baylor Coll. Med., Houston) and J. L. Melnick. *J. Nat. Soc. Exp. Biol. Med.* 113(2):339-341, 1963.

Adenovirus type 7, passaged 5 times in Rhesus monkey kidney cells had an av. adenovirus titer of 10^{3.6} TCID₅₀/ml and an adenovirus particle count of 10^{7.6} particles/ml. The same stocks had an av. SV40 titer of 10⁶ TCID₅₀/ml and an SV40 particle count of 10⁹ particles/ml. When the virus stock was heated at 50°C for 30 min. in distilled water, the adenovirus component lost all of its infectivity and a large part of its antigenicity when 0.2 ml was inj. into rabbits. After similar treatment, the SV40 component retained both infectivity and antigenicity. When the virus stock was heated at 50°C for 30 min. in M magnesium chloride, the adenovirus component lost all its infectivity but retained all its antigenicity; the SV40 component was induced both in infectivity and antigenicity.

63-716 MULTIPLICITY OF CELL RESPONSE TO THE BAI STRAIN A (MYELOBLASTOSIS) AVIAN TUMOR VIRUS. V. ELABORATION OF VIRUS BY PANCREAS OF CHICKENS INOCULATED WITH THE AGENT. (E.) Heine, U. (Dept. Surg., Duke U. Med. Ctr., Durham, N. C.), G. De Thé, D. Beard and J. W. Beard. *J. Nat. Cancer Inst.* 30(4):817-835, 1963.

No virus particles were detected on electron microscopic examination of the pancreas of 11 normal chicks, or in that of 10 hosts with erythroblastosis induced by strain R virus or of 6 chicks with erythroblastosis induced by ES4 strain virus. After induction of myeloblastosis by the BAI strain A virus, the pancreas of 5/14 birds contained virus particles. Budding occurred in 4 of these hosts and also in the pancreas of 4/12 chicks that received transplants of BAI-strain-A induced nephroblastoma, whether or not there was growth.

63-717 CORRELATION OF HISTOLOGIC FEATURES WITH VIRAL CONTENT OF SHOPE PAPILLOMAS OF COTTONTAIL RABBITS. (E., Abstract) Evans, C. A. (Dept. Microbiol., U. Wash., Seattle), A. L. Rashad and N. K. Mottet. *Bact. Proc.* 1963:153.

Tumors induced by Shope papilloma virus (Washington 8 strain, 5 or 50 ID₅₀), removed 6, 12, and 18 wk. after inoc. onto 8 skin sites on each of 8 cottontail rabbits, were assayed for their virus content and studied histologically. In 13/45 specimens the viral content (ID₅₀/g of tumor tissue) was low (1,000 or less), in 16/45 it was high (100,000-10,000,000), and in 16/45 intermediate. The several tumors on a given animal at a given time had approx. the same viral content. Partially regressed tumors showed a high viral content. Tumors with high virus content showed basophilia of the superficial epithelium, and cells of the granular and horny layers; fibrillar fragmentation was also seen. Low-viral-content tumors showed the same changes but to a lesser degree and the intracellular basophilic granules were smaller.

63-718 EFFECT OF CELL-FREE EXTRACTS OF PS TUMORS ON MICE OF THE SAME STRAIN. (Fr.) Mouriquand, C. (Pasteur Inst. Lyon, France), J. Mouriquand, J. Terrier and B. Martinet. *Ann. Inst. Pasteur (Paris)* 104(4):460-468, 1963.

Cell-free extracts from spontaneous mammary tumors, lymph nodes, and spleens from 8 spontaneous leukemias or from a leukemia induced in a male by inj. of brain extract (all from the PS mouse strain), were inj. s.c. or i.p. into 24-48-hour-old PS mice. Only 208/644 inj. animals survived to adulthood, 296 died in infancy and 40 more died before 5 mo. of age due to various benign conditions. The remaining animals, 97 males and 111 females, were observed for up to 22 mo.

The incidence and latency of tumors in females, experimental and controls, resp., was: mammary 40.5% (11.7 mo.) and 43.1% (11.4 mo.); leukemias 32% (12.7 mo.) and 35.5% (13.2 mo.); and in a fibrosarcoma of the abdominal wall and a malignant tumor of the ovary 1.8% (15.7 mo.), controls, none. Among males the tumor incidence and latency for experimental and controls were: leukemias 27% (13.3 mo.) and 4.5% (9.7 mo.), other neoplasms; 1 fibrosarcoma, 2 skin epitheliomas, 2 hemangio-endotheliomas, 1 malignant salivary tumor, 1 malpighian epithelioma of the skin, 1 glandular epithelioma of the lung, 8% (15 mo.) and none in controls. Among males there were 4 deaths: from a possible lymphosarcoma of the lymph nodes, 2 adenopathies, and 1 chronic nephritis associated with splenic amylosis. The leukemias showed unusual hyperbasophilia of lymphoblasts, and a tendency toward plasmoblastic evolution. In the males the high incidence of leukemias was observed in animals receiving either mammary or leukemic tumor cell-free extracts. The data suggest that in males inj. of tumor extracts activates a latent process, possibly a provirus, which is spontaneously expressed in females due to favorable hormonal conditions.

- 63-719 ATTEMPTS TO TRANSMIT FRIEND VIRUS LEUKEMIA WITH SUB-VIRAL CONSTITUENTS. (E., Abstract) Rich, M. A. (Lab. Cancer Res., Albert Einstein Med. Ctr., Phila.), J. E. Geldner, R. Siegler and J. Gershon-Cohen. Bact. Proc. 1963:154.

Swiss mice (20) were inoc. with extracts from infected spleens which contained RNA 500 µg/ml, DNA 300 µg/ml, and protein 220 µg/ml. After 4-9 mo., malignant lymphoma developed with splenomegaly, adenopathy, anemia, thrombocytopenia, and leukocytosis with atypical lymphocytes. When lymph node and spleen were serially transplanted into weanling Swiss mice, similar disease was induced in 7/30 mice in 2-3 mo. (to date); but this disease differed from Friend disease in latency, pathology, and in the absence of the characteristic preleukemic splenic hyperplasia. Electron microscopy revealed budding 80-90 mµ particles in the lymph node, spleen and thymus which were characteristic of murine leukemia viruses; similar smaller, tailed particles were found in blood concentrates. The original chemical extraction did not rigorously exclude the presence of whole virus, Friend or other.

- 63-720 COMPARATIVE STUDIES ON HIGHLY PURIFIED TUMORIGENIC AND NON-TUMORIGENIC STRAINS OF ADENOVIRUS. (E., Abstract) Green, M. (Dept. Microbiol., St. Louis U. Sch. Med.) and M. Pina. Bact. Proc. 1963:159

Highly purified type 12 adenovirus, at conc. of 0.2-5 µg, inj. intrapulmonarily induced pulmonary sarcomas and dark, patchy livers and death in

newborn hamsters within 3-8 wk.; after s.c. or i.p. inj., abdominal tumors were found. Higher doses, 5-100 µg, often brought death in several days; survivors were often runted. Similarly purified type 2 adenovirus, even at ten times the above conc., showed no tumor formation, although high concentrations (5-100 µg) often brought death in several days. Both viruses had 12-13% DNA (of DNA + protein) and similar amino acid composition but differed markedly with regard to base composition, buoyant density, and denaturation temperature.

- 63-721 SERIAL CELL-FREE PASSAGE IN RATS OF THE MOUSE LEUKEMIA VIRUS. EFFECT OF THYMECTOMY. (E.) Gross, L. (Cancer Res. Unit, VA Hosp., Bronx, N. Y.). Proc. Soc. Exp. Biol. Med. 112(4):939-945, 1963.

Passage A leukemia virus, initially isolated from spontaneous Ak mouse leukemia and passed serially through newborn C3H mice, was also found to be pathogenic for suckling Sprague-Dawley or Osborne-Mendel rats; although the incidence of leukemia in rats was only 56-89% in the first passage (av. latent period of 3-4.2 mo.), after 1-2 passages it increased to practically 100% and the latent period decreased to less than 3 mo. All rats died 1-2 wk. after diagnosis of leukemia. The virus was also still pathogenic for mice after 3-7 passages in rats. Most rats developed lymphatic or stem cell leukemia (leukemic or aleukemic), and about 7% developed myelocytic leukemia; in addition, lymphosarcomas were common, and reticulum cell sarcomas were also seen, as well as Hodgkin-like lesions in the lymph nodes and spleen. When rats were thymectomized approx. 1 wk. after virus inoc., the development of leukemia was delayed slightly (from av. of 2.8 to 4 mo.) and the incidence of myelocytic leukemia was increased from 6 to 14.6%; in addition 1 thymectomized rat developed erythro-myeloid leukemia. Incidence was 100% in controls and 90-96% in treated animals. For related work see CRA 1(1):#100, 1963.

- 63-722 THE HISTOCHEMISTRY OF INCLUSIONS IN TUMOUR CELLS. (E.) Kakulas, B. A. (Dept. Path., U. Western Australia, Perth) and D. G. A. Gibb. J. Path. Bact. 85(2):457-465, 1963.

Histochemical study of cell inclusions occurring in routine biopsy and necropsy material of tumor cells from 10 pts. revealed inclusions in 7/10 to be protein: in 4 of the 7 cases amino, tyrosyl, sulphhydryl and disulfide terminal groups were identified; in 3 pre-keratin, mucoprotein and a mucopolysaccharide associated with protein were present. Inclusions of 3/10 could not be identified. Autofluorescence, birefringence, calcium, iron, Hb, Hb-derivatives and ribonucleic acid were absent in all cases. The Feulgen reaction was negative in all except the control (molluscum contagiosum). The inclusions are believed to be

the result of disordered protein metabolism, and are not related to presence of a virus.

63-723 PROPERTIES OF HAMSTER EMBRYO CELLS TRANSFORMED IN VITRO BY POLYOMA VIRUS.

(E., Abstract) Defendi, V. (Wistar Inst., Philadelphia, Pa.) and J. Lehman. Proc. Am. Assn. Cancer Res. 4(1):15, 1963.

Hamster embryo cells infected with polyoma virus and carried in mass cultures undergo morphological changes within 40-60 days. Analyses of 6 cell lines at regular intervals revealed no common pattern of development, each one varying by one or more properties from the others (presence of virus, morphology, karyotype, s.c. transplantability into adult hamsters, and antigenic composition). Morphological changes preceded transplantability, even though all cell lines eventually were transplantable at low cell doses (10^2 - 10^4 cells). There was no definite correlation between chromosomal changes and transplantability. These cells were indistinguishable from a spontaneous cell line except for persistence of infectious virus and various degrees of loss of contact inhibition. See also CRA 1(3):#583, 1963.)

63-724 PROGRESS WITH SOME TUMOR VIRUSES OF CHICKENS AND MAMMALS: THE PROBLEM OF PASSENGER VIRUSES. (E.) Negroni, G. (Div. Exptl. Biol. Virol., Imperial Cancer Res. Fund, London). Pp. 515-561 in Advances in Cancer Research, Vol. 7. Haddow, A. and S. Weinhouse (Eds). New York, Academic Press Inc., 1963.

In this review the author has attempted to summarize those approaches to the problem of oncogenic viruses which seem most promising. The ultrastructure, biochemical, physicochemical, and immunologic properties of Rous sarcoma virus are dealt with in connection with cells, its pathogenicity for birds and mammals and behavior in in vitro experiments. In a section on avian leukoses are reviewed erythroleukosis, myeloblastosis, lymphoid leukosis, MH2, Fujinami renal tumors. Rabbit tumor viruses considered are those that produce fibromata and papillomata. The major portion of the review is devoted to mouse tumor viruses (MTA, Gross's, Friend's, Moloney's, Schwartz's leukemic, Graffi's disease, polyoma virus and SV40. This section concludes with a discussion of non-oncogenic viruses associated with tumors (Toolan's, Galus Adeno-like and Riley's agent). It is stressed that much of the information is derived from the work on polyoma virus carried out both in vitro and in vivo. While much information on tumor viruses has been accumulated which can aid in the detection of viruses, one must be cognizant of the difficulties in deciding if a virus isolated from a tumor is really the cause of the tumor itself. Only the chicken and rabbit tumor viruses and the leukemia virus in mice reproduce the tumors from which they were originated.

63-725 STUDIES ON THE INDUCTION AND MECHANISM OF IMMUNITY IN THE NATURAL HOST TO A MURINE LEUKEMIA VIRUS. (E., Abstract) Fink, M. A. (NCI, Bethesda, Md.). Proc. Am. Assn. Cancer Res. 4(1):19, 1963.

BALB/c mice were inj. i.p. with Freund's adjuvant mixed with either heat (56°C for 30 min.) or formalin (0.1%) treated murine leukemia virus; after 3 wk. a s.c. inj. was given without the adjuvant. When inj. with live virus, the mice inj. with formalinized virus showed solid immunity; those inj. with heat treated virus showed a much lesser degree of immunity. Study of circulating antibody levels paralleled these findings. This suggests the immunity is due to circulating antibody, which is supported by failure of the survivors from the immunized group to show a delayed hypersensitivity as indicated by intradermal testing.

63-726 TRANSPLANTATION OF FRIEND VIRUS-INDUCED MOUSE LEUKEMIC CELLS TO THE HAMSTER

BRAIN. (E., Abstract) Burnstein, T. (Sch. Vet. Sci. Med., Purdue U., Lafayette, Ind.) and M. Stromberg. Fed. Proc. 22(2):324, 1963.

Friend's transplantable solid tumor, converted to ascites form and passed serially in DBA/2 mice was transplanted into the brain of day-old hamsters. The tumor heterografts grew extensively for about 2 wk., during which time 2/3 of the recipients died. Surviving animals rejected the transplant and showed destruction and clearance of the cells from the brain. Concurrent with the growth and rejection of the cells a severe hydrocephalus developed in survivors. The hydrocephalus was not observed following transplantation of lysed cells, normal mouse cells, or virus alone, suggesting that it is a consequence of tumor cells. Persistence of the virus in the heterologous host paralleled that of the tumor cells.

63-727 DEVELOPMENT OF ESTABLISHED MOUSE LINES AND THEIR TRANSFORMATION BY POLYOMA VIRUS. (E., Abstract) Todar, G. J. (NYU Sch. Med., New York, N. Y.) and H. Green. Fed. Proc. 22(2):382, 1963.

Two lines of Swiss mouse embryo cells developed under cultural conditions that did not allow formation of a confluent monolayer, possessed an unusually high degree of contact inhibition. Cell growth was completely stopped when the monolayer was completed and there was no growth out of the monolayer. One of these lines was much more sensitive than freshly cultivated mouse embryo cells to the cytotoxic effect of polyoma virus while being transformed to a much higher efficiency. The line appears well suited for in vitro studies of viral transformation.

- 63-728 EXPERIMENTAL INDUCTION OF SPLENOMEGALY AND ERYTHROCYTOPOIESIS BY A MURINE VIRUS. (E., Abstract) Philp, J. R. (Dept. Pathol., U. Oregon Med. Sch., Portland), W. Weaver, T. Fujikura and B. V. Siegel. Fed. Proc. 22(2):488, 1963.

In BALB/c mice i.p. inoc. with Rauscher virus caused little or no morphologic change until 7 days, when spleens began to show nests of hyperplastic reticulum cells and erythropoiesis in the peripheral sinusoids. No lesions were found in other organs including liver, kidney, lung, thymus, or bone marrow. Between 19 and 37 days reticulum cell hyperplasia and erythropoiesis of the spleen became more marked and at this stage nests of hyperplastic reticulum cells and erythropoiesis were recognized in liver and lung. Bone marrow, however, showed cellular hypoplasia, particularly of the erythrocytic series.

- 63-729 ASSIMILATION OF AMINO ACID ANALOGUES BY A VIRAL INDUCED TUMOR. (E., Abstract) Love, W. C. (Depts. Pharmacol. Microbiol., Ind. U. Sch. Med., Indianapolis) and A. S. Levine. Fed. Proc. 22(2):615, 1963.

Rous tumor slices harvested 5-6 days after inoc. of the Bryan strain of Rous virus onto dropped chorioallantoic membrane (CAM) of 10-12-day-old embryonated chicken eggs concentrated C^{14} - α -aminoisobutyric acid (AIB; 0.05 μ C/ml) to 4.44 (CPM/ml intracellular water:CPM/ml medium water) in 4 hr. Control CAM concentrated AIB to 2.38 during the same period of time. After incubation with l-aminocyclopentane-l-carboxylic acid, tumor slices also accumulated cycloleucine. The increased conc. of amino acids by Rous sarcoma slices may be related to a previously reported increased rate of amino acid incorporation into tumor proteins.

- 63-730 BIOCHEMICAL CHARACTERISTICS OF TUMORIGENIC STRAINS OF HUMAN ADENOVIRUS. (E., Abstract) Green, M. (Dept. Microbiol., St. Louis U. Sch. Med., Mo.), M. Piña and H. Polasa. Fed. Proc. 22(2):645, 1963.

A highly purified type 12 adenovirus was isolated and found to cause tumors in newborn hamsters with as little as 0.2 μ g of the virus. The type 12 adenovirus DNA had a melting point (MP) of 88-89° C and a CsCl buoyant density of 1.710, whereas a non-tumorigenic type 2 adenovirus had a MP of 93° C, and a density of 1.718. Both viruses had

a buoyant density of 1.33-1.34 in RbCl, 12-13% DNA (of DNA + protein), no demonstrable RNA and similar amino acid compositions. Differences were found between the amino acid composition of host cell protein and viral protein.

- 63-731 PARTIAL PURIFICATION OF A MOUSE LEUKEMOGENIC AGENT. (E., Abstract) Humphrey, G. B. (Argonne Cancer Res. Hosp., U. Chicago, Ill.). Fed. Proc. 22(2):674, 1963.

A cell-free supernatant from the ascitic fluid of leukemia induced in AKR mice by i.p. inoc. of the L 4946 lymphatic leukemia, caused ascitic leukemia and death within 3-4 wk. when inj. into adult C57BL mice. The cell-free supernatant was leukemogenic after centrifugation at 125,000 x g for 1 hr., but was inactive after passage through bacterial filters, after heating at 60° C for 10 min., or after freezing and thawing. A saline insoluble component of the first ethanol precipitate of these leukemogenic supernatants was also leukemogenic. It contained protein and RNA, but no detectable DNA. As little as 0.04 mg protein and 0.002 mg RNA from this fraction produced lymphatic leukemia and death in adult mice. The saline insoluble material was resistant to RNase, DNase, and lysozyme, but was inactivated by trypsin, by heating at 60° C for 10 min., or by freezing and thawing.

- 63-732 REPLICATION OF SPECIFIC VIRAL ANTIGEN IN ADENOVIRUS TYPE 12 TUMOR TRANSPLANTS. (E., Abstract) Huebner, R. J. (NIH, Bethesda, Md.), W. T. Lane, J. Reynolds and H. C. Turner. Fed. Proc. 22(2):438, 1963.

A number of primary adenovirus-induced cancers were transplanted successfully in weanling and newborn hamsters. Sera taken at 20-25 days were uniformly negative for complement fixing serum antibodies to adenovirus 12 antigen and to common adenovirus antigens. However, all animals developing visible tumors also developed complement fixing antibodies to the adenovirus 12 antigen, and most of the hamsters who failed to develop tumors also failed to develop complement fixing antibodies. Rises in specific complement fixing antibody were only rarely associated with detectable rises in neutralizing antibody. The specificity of the serologic reactions implies that the rise in specific complement fixing antibodies which accompanies replication of cancer cells must be mediated by replicating genetic material of the virus.

See also abstract nos.: 593, 598, 603, 612, 679, 698, 740, 743

EPIDEMIOLOGY AND BIOMETRY

63-733 THE TEN LEADING CAUSES OF DEATH.
INTRODUCTORY NOTE. (E. and Fr.)
Epidem. Vital Statist. Rep. 16:30-77, 1963.

In 1960, malignant neoplasms (which caused 18% of all deaths) were the second most frequent cause of death in Canada, USA, Denmark, Finland, France, Western Germany, the Netherlands, Norway, Sweden, Switzerland, the United Kingdom, and Australia; heart disease accounted for approximately 33%. The percentage of all deaths which was due to cancer ranged from 15% in Australia to 22% in the Netherlands and Denmark. The median cancer death rate per 100,000 population was approximately 177 (vs. 162 in 1954-56), ranging from 129.4 in Australia to 215.9 in England and Wales. The percentage of all deaths which was due to cancer was tabulated in 1954-56 and 1960 (in that order), as follows: Canada, 15.8-16.6; U.S.A., 15.8-15.6; Denmark, 21.6-22.0; Finland, 16.0-17.4; France, 15.1-17.3; Western Germany, 17.7-18.3; Netherlands, 20.6-22.1; Norway, 18.6-18.1; Sweden, 17.2-18.5; Switzerland, 18.8-19.3; England and Wales, 17.8-18.8; North Ireland, 14.7-15.7; Scotland, 17.2-17.9; Australia, 14.3-15.0; Japan, 11.0-13.3, resp. In Colombia and Ceylon, where cancer was the 7th most frequent cause of death, they were 2.6-2.6 and 1.7-2.6, resp. Increases of more than 2% in particular age groups were as follows: age 1-4- Finland (3.3), France (2.8), Norway (3.5), Sweden (4.1); age 5-15- France (3.0), Denmark (7.2), Netherlands (3.0), Australia (3.0), Japan (2.8); age 15-44- France (2.2), Norway (2.5), Sweden (2.6), Scotland (2.6), Japan (2.7); age 45-64- France (4.1), Sweden (2.9), Ceylon (2.7), Japan (2.5). Age 65 and over, none.

63-734 LUNG CANCER. (E.) Antell, M. J.
(St. Vincent's Hosp., Bridgeport,
Conn.) and R. W. Berry. *St. Vincent Hosp. Med. Bull.* (Bridgeport) 4(1):14-20, 1962.

Among 106 cases of histologically proven lung cancer diagnosed and treated at the authors' hospital between 1955 and 1961, there were 94 males and 12 females. Among the females, there were 3 adenocarcinomas, 5 epidermoid or squamous cell carcinomas and 4 undifferentiated, compared to 73 epidermoid, 7 anaplastic, 5 adeno- and 18 undifferentiated carcinomas among the men. The predominant age group was 50-70 yr. (68 men, 6 women). None of the women gave a history of smoking, while the men consumed an av. of 37 cigarettes/day for an av. of 35 yr. The authors do not further discuss the etiology of lung cancer, being more interested in its early diagnosis and treatment and the final outcome, which is still discouraging.

63-735 TROPHOBLASTIC DISEASES IN TAIWAN.
A REVIEW OF 157 CASES IN A 10 YEAR
PERIOD. (E.) Wei Ping-Yen (Dept. Obstet.

Gynec., Natl. Taiwan U. Coll. Med., Taipei) and
Ouyang Pei-Chuan. *Am. J. Obstet. Gynec.* 85(7):
844-849, 1963.

Incidence of trophoblastic disease in Taiwan was higher than in Western countries. Between 1951-60, 157 cases were observed, an incidence of 1 in 82 pregnancies. Of these, 103 were hydatidiform moles (HM), 23 chorioadenoma destruens (CAD), 26 choriocarcinomas (CC), 3 syncytial endometritis and 2 unclassified cases. Progression to CC occurred in 2.3% of pts. with HM and 4.3% of pts. with CAD. The incidence of disease appeared disproportionately higher in the age group over 40 and in the parity group of over 6.

63-736 CARCINOMATOUS DEGENERATION IN SEBACEOUS
CYSTS. (E.) Koontz, A. R. (Baltimore,
Md.). *Am. J. Surg.* 105(5):677-679, 1963.

In the case report of a 64-year-old woman who developed a huge, fungating, squamous cell carcinoma of the scalp at the site of an ulcerated sebaceous cyst, the author points out that the pt.'s daughter, father, paternal grandfather and the latter's mother all had multiple sebaceous cysts of the scalp, indicating a familial tendency. Since data in the literature indicate malignant degeneration of up to 4.3% of such cysts, early excision is recommended.

63-737 OBSERVATIONS ON FREQUENCY OF CARCINOMA
OF THE PENIS AT MACASSAR AND ITS
ENVIRONS (SOUTH CELEBES). (E.) Tan, R. E.
(Stella Maris Hosp., Macassar, Indonesia). *J. Urol.* 89(5):704-705, 1963.

The age distribution of pts. with penile carcinoma observed in the Mohammedan population of Macassar, who are circumcised at age 5-10 yr., was: 22-30 yr., 6; 31-40 yr., 12; 41-50 yr., 9; 51-60 yr., 6; 61-70 yr., 1; and unknown age, 12. The incidence was 1/20,000. There were also 2 penile carcinomas in uncircumcised Chinese in Macassar, giving an incidence of 1/10000. The data suggest that circumcision done late in childhood or in advanced age, as is the custom for the Mohammedans in Macassar, does not affect the incidence of carcinoma of the penis when compared with the uncircumcised Chinese.

63-738 FAMILIAL AGGREGATION OF LUNG CANCER
AMONG HOSPITAL PATIENTS. (E.)
Tokuhata, G. K. (John Hopkins U., Baltimore) and
A. M. Lilienfeld. *Public Health Rep.* 78(4):277-
283, 1963.

Reported is an extension (with larger numbers of pts. and controls) of a work previously abstracted (see CRA 1(1):#128, 1963).

- 63-739 THE ROLE OF TRAUMA IN THE AETIOLOGY OF TESTICULAR NEOPLASMS. (E.) Field, T. E. J. Roy. Army Med. Corps 109(1):58-61, 1963.

A group of 135 army pts. with malignant testicular tumors were questioned regarding any history of injury to the testicle. A definite history of injury, usually preceding the appearance of other symptoms such as testicular enlargement, was given by 27/135. In this group, 17/27 pts. had a history of very recent injury, whereas the remaining gave histories of trauma several mo. or yr. previously. Only 4/27 pts. reported pain accompanied by nausea at the time of injury, suggesting that tumor had already replaced normal tissue.

- 63-740 MULTIFOCAL LYMPHOMA IN SOUTH AFRICA. ITS FIRST OBSERVATION IN SOUTH AFRICA AND IN WHITE CHILDREN. (E.) Gluckman, J. (Clin. Labs., Med. Centre, Johannesburg, S. Africa). S. Afr. Cancer Bull. 7(1):7-12, 1963.

A form of malignant lymphoma, resembling lymphosarcoma and occurring only in African children within a roughly defined area extending across Central Africa from Gambia to Tanganyika and Mozambique, has reportedly failed to occur previously above an altitude of 5,000 ft. or in cold climates. However, 3 cases occurred in white children in the Transvaal Highveld area, at altitudes of 4990-6000 ft. The author speculates that the disorder may be due to a virus conveyed by a vector which has moved steadily southward since the disorder was first described in 1953. All the 3 children had been down to sea level on 1 or more occasions, although not into malarial areas. A 4th case has been reported in an African child; and 2 other possible cases were reported in the USA (1 in a child who came from Africa). See also the following abstract.

- 63-741 EDITORIAL. THE MULTIFOCAL LYMPHOMA SYNDROME IN SOUTH AFRICA. (E.) S. Afr. Cancer Bull. 7(1):1-3, 1963.

In an editorial discussion of the syndrome reported in CRA 1(4):#740, 1963, is reviewed Burkitt's original distribution data, which eliminated areas with less than 20 inches of rainfall per yr. and those in which seasonal mean temperature fell below 60°F. The possibility that the disorder was contracted during holiday visits to the Natal and Cape Coasts is questioned, especially in the absence of reports of indigenous cases in the S. African littoral. It is suggested that a skeptical approach should be taken to the concept of a vector-borne virus as the source of this tumor. (See also CRA 1(3):#467, 1963.)

- 63-742 CYTOLOGY AND HISTOCHEMISTRY OF THE BURKITT LYMPHOMA. (E.) Wright, D. H. (Makerere U. Coll. Med. Sch., Kampala, Uganda). Brit. J. Cancer 17(1):50-55, 1963.

A cytological and histochemical study of 25 cases of the Burkitt tumor supports the classification as a lymphoma. The uniformity of cytological and histochemical pattern does not justify the separation of the Burkitt tumor into different histological types. This cytological uniformity fits better with the present concept of the Burkitt tumor as a single entity possibly induced by an arthropod born virus.

- 63-743 BURKITT-TYPE LYMPHOSARCOMA. (E., Abstract) Bennett, M. B. (Dept. Radiother., Groote Schuur Hosp., Observatory Cape, U. S. Africa) and L. Anstey. S. Afr. Med. J. 37(17):476, 1963.

Of 43 cases of lymphomata reviewed in Cape Town hospitals since 1951, 6 fit the clinical and histological description of Burkitt. The 6 cases comprise 2 white and 4 Cape colored children.

- 63-744 CELLULAR DEGENERATION ASSOCIATED WITH CHARACTERISTIC NUCLEAR FINE STRUCTURAL CHANGES IN THE CELLS FROM TWO CASES OF BURKITT'S MALIGNANT LYMPHOMA SYNDROME. (E.) Epstein, M. A. (Middlesex Hosp. Med. Sch., London) and P. B. Herdson. Brit. J. Cancer 17(1):56-58, 1963.

Jaw tumor biopsy samples from 2 boys (aged 5 and 6) with Burkitt's lymphoma showed, on electron microscopy, early, nonspecific degenerative changes. Characteristic nuclear features included marginated chromatin masses, spherical granular bodies of about 1.5 μ in diameter, and aggregation of dense particles about 15 m μ in diameter. This close association of nuclear with other (early) degenerative changes indicates that the nuclear phenomena are probably a manifestation of cytolysis in the malignant cells, rather than any indication of the presence of a virus.

- 63-745 A SURVEY OF CANCER MORTALITY AT DETROIT OSTEOPATHIC HOSPITAL. (E.) Fox, A. R. (Detroit Osteopath. Hosp., Michigan). J. Am. Osteopath. Assn. 62(7):573-580, 1963.

Cancer-death rates (per 100,000) in Wayne County, Mich., as indicated by death certificate statistics for 1950 and 1960, resp., included a decrease of gastric cancers from 15.8 to 13.6; an increase of cancers of the intestine from 13.7 to 16.9, respiratory tract from 16.5 to 25.2, prostate from 5.1 to 7.6, lymphatic and hematopoietic systems from 6.0 to 8.3, and leukemia from 4.8 to 5.7. In the state of Michigan, as a whole, the death rates included a decrease of gastric cancer

from 16.9 to 12.4; an increase of cancers of the respiratory tract from 12.6 to 20.1. Changes in death rates due to other specific cancer loci in Michigan State or for Wayne Co. were insignificant (i.e., less than 2/100,000). In Wayne Co., cancers which were not classified in terms of site increased from 33.7 to 41.3, during the same interval; in the State of Michigan as a whole, from 36.0 to 38.1. The overall death rate due to cancers of all types, in Wayne Co., rose from 135.8 to 159.8; in the state as a whole from 136.3 to 144.8. Complementing these general data is a detailed survey of cancer mortalities occurring at the Detroit Osteopathic Hospital.

746 A CRITICAL LOOK AT STATISTIC EPIDEMIOLOGY. (E.) Wilson, E. B. (Office of Public Health Res., Boston, Mass.). Cancer 16(4):510-515, 1963.

The author presents a detailed statistical review of 5 epidemiological studies reported in the literature, the author questions the validity of both sampling methods and methods of analysis which appear to support the thesis of a relationship between the incidence of cervical cancer in different groups and various medical and sociologic factors.

747 REPORT OF 1,160 REGISTERED TUMOR CASES IN PAPUA AND NEW GUINEA. (E.) Farago, G. (Tumor Registry Territ. Papua and New Guinea, Port Moresby, Papua). Cancer 16(5):570-580, 1963.

The author reviews 1,160 cases of malignant tumors registered between 1958-1962 in Papua and New Guinea. The incidence of registered tumors for the age group 0-9 was 7.16%; 10-19, 10.5%; 20-29, 13.97%; 30-39, 26.38%; 40-49, 24.24%; 50-59, 16.12%; over 60, 5.08%. The incidence (number of pts.) of the most common forms of cancer in both sexes exclusive of primary cancer of the liver was cancer of the oral cavity, 210; skin, 189; digestive system, 183; female genitalia, 103; malignant lymphoma and leukemia, 96; and cancer of the breast (females), 52. The anatomical localization of 19 skin cancers (159 squamous cell, 11 basal cell carcinomas and 19 melanomas) was head and neck, 21; trunk, 23; upper extremities, 6; lower extremities, 100; and foot, 39. Tumors of the oral cavity had an incidence similar to that in Asiatic countries: 129/130 were betel nut chewers; smoking was common. A 14.4:1 ratio of squamous cell carcinoma to basal cell carcinoma with the localization of the former predominantly below the knee in association with chronic tropical ulcers was recorded. Tumors of the digestive tract, central nervous system and leukemia may not have been diagnosed. The incidence of lung cancer was low.

63-748 LEUKEMIA IN CHILDREN. INCIDENCE, CLINICAL MANIFESTATIONS, AND SURVIVAL IN AN UNSELECTED SERIES. (E.) Meighan, S. S. (Cleveland Clin., 605 High St., Oregon City). Cancer 16(5):656-664, 1963.

The incidence of childhood leukemia was 2.84 per 100,000 in Saskatchewan between 1948-60, inclusive. Of 106 pts., 94 had acute lymphatic, 8 acute myeloid, 3 acute monocytic, and 1 chronic myeloid leukemia. The male to female ratio was 1.4:1. Peak incidence occurred between ages 2-4 yr. The clinical findings (including survival) compare unfavorably with other reports probably because the series includes an unselected group of children from which no child was eliminated. In the future all such studies should state the methods employed in collecting data; mean and median survival figures should be given from the time of diagnosis.

63-749 THE DEVELOPMENT OF MALIGNANT LYMPHOMA IN PATIENTS WITH SJÖGREN'S SYNDROME. (E., Abstract) Talal, N. (Bethesda, Md.) and J. J. Bunim. Arthritis Rheum. 6(3):302, 1963.

Among 58 pts. with Sjögren syndrome, 3 developed reticulum cell sarcoma and a 4th developed lesions resembling those of Waldenström's macroglobulinemia, after a duration of illness of 4-10 yr. Seen in at least 3/4 were accompanying splenomegaly, purpura, vasculitis, leukopenia, lymphopenia, high-titer rheumatoid factor, and abnormal tissue antibodies. Prior X-ray therapy to the parotid glands had been employed in 3/4 of this group, whereas of the remaining 54 (who did not develop malignancies); only 1 had been exposed to radiotherapy.

63-750 FURTHER STUDY IN AETIOLOGY OF CARCINOMAS OF THE UPPER ALIMENTARY TRACT. (E.) Shanta, V. (Cancer Inst. (W. I. A.), Madras, India) and S. Krishnamurthi. Brit. J. Cancer 17(1):8-23, 1963.

The relative frequency of carcinoma of the upper alimentary tract was 34% in Madras and 35.9% in Bombay. Of 882 pts. (682 males, 254 females), compared to 400 controls (300 males, 100 females) the site incidence as per cent of all upper alimentary cancers were lip, 2.1%; buccal mucosa (B), 50.5%; anterior 2/3 of tongue, (AT), 9.9%; posterior 1/3 of tongue (PT), 6%; palato-glossal fold, 2%; pharynx (Ph), 15.5%; hypopharynx (HX), 1.5% and esophagus, (E), 12.5%. Cancer of the upper alimentary tract accounted for 40.29% of all malignancies; that of the B, 19%. Betel nut and tobacco chewing was the habit of 83% of males and 85% of females with cancer of the lip and B; 73.9% of males and 50% of females with cancer of the AT; 43.85% of males and 75% of females with cancer of the PT; 35% of males and 43.5% of females with cancer of the Ph; 27.7% of males

and 8.3% of females with cancer of the HX; and 42.1% of males and 13.9% of females with cancer of the E; compared to controls, 9.2% of males and 11.2% of females. Heavy use of tobacco in some form for over 20 yr. was reported for 100% of males with lip cancers, 98% of B cancers; 92.8% of AT cancers; 98% of PT cancers; 94.7% of oropharyngeal cancers and 82.5% of E cancers; such usage in controls was 60.9%. Comparable values for females were 85.7% (lip); 89% B; 66.7% AT; 100% PT; 60% Ph; and 52.9% E, resp.; controls, 11.2%. Dental sepsis was present in approximately 90% of the study group and controls of both sexes; sideropenia in 100% of females with cancer of the HX and cervical E. Exclusion of tobacco chewers lowered the frequency of oral carcinoma to 3.8%, a figure comparable to the frequency in western countries. The fact that females were virtually nonsmokers accounted for the lower incidence of cancer of the upper alimentary tract in them. Hormonal patterns, heredity, race, environment, occupation, pre-existing diseases and pathology were of no etiological significance.

- 63-751 THE ALLEGED RARITY OF CANCER IN THE FAR EAST. (E.) Muir, C. S. (U. Singapore Gen. Hosp., Singapore). *Cancer* 16(6): 812-818, 1963.

Factors conducive to the erroneous belief that cancer is rare in the Far East include high death rate from other diseases, failure to appreciate differences in the age-structure of populations, various cultural and social barriers to the acceptance of western medical care and insufficient medical facilities. The age-standardized death rates for Singapore per 100,000 for all cancers from 1957-58 were for males age 0-34, 8.9; age 35-64, 221.8; age 65+, 643.6; for all ages, 142.6; for females age 0-34, 6.4; age 35-64, 146.9; age 65+, 319.2; for all ages, 85.2.

- 63-752 MALIGNANT NEOPLASMS AMONG ALASKAN NATIVES: AN EPIDEMIOLOGICAL APPROACH TO CANCER. (E.) Torrey, E. F. *McGill Med. J.* 31(3):107-115, 1962.

For the fiscal years 1958-61, 170 malignant neoplasms were registered at Alaska Native Health Service hospitals. The cancer death rate for the native population was 75/100,000; one-half that of the U.S. as a whole. The incidence of cancer of the esophagus was 4.1%; stomach, 4.7%; intestines, 8.3%; breast, 8.8%; central nervous system, 1.2%; thyroid, 2.9%; bone, 1.8%; lymphosarcoma, 1.2; leukemia, 3.8% and rectum, lung primary, ovary, prostate, and skin, 2.3% each. The incidences of 2 cancers was greater than that expected by a factor of about 3: cervix (16.5%) and kidney (7.1). Division into 3 racial groups (97 Eskimos, 51 Indians, 22 Aleuts) produced slight but

statistically insignificant differences. Eskimos accounted for 44 of 54 cancers of digestive organs, Indians only 4; Indians accounted for 10/15 cases of breast cancer, 7/12 of kidney cancer and 5/6 of cancer of the male genitalia. The incidence in half-bloods (15%) was significantly lower than in full-bloods. Attempts to correlate incidence with residence in population centers did not produce significant results. The author believes that the findings can most readily be explained by a carcinogen theory.

- 63-753 GEOGRAPHICAL PATHOLOGY OF CANCER OF THE PENIS. (E.) Riveros, M. (Fac. Med. Sci., Nat. U. Paraguay, Asuncion) and R. F. Lebrón. *Cancer* 16(6):798-811, 1963.

Penile cancer ranks 5th in frequency among all malignant tumors observed in the Tumor Clinic of Asuncion, Paraguay and 4th among pathological material studied by the Inst. of Path. Among 168 pts., tumor frequency according to age was: 36.9%, 60-70; 21.4%, 50-60; 18.5%, 70-80; 11.9%, 40-50; 7.7%, 30-40. Of all penile cancers, 85.72% were in rural pts., farmers, and persons belonging to a substandard socioeconomic class, the majority of whom had poor sexual habits, and inadequate hygiene. The greater number of the pts. had a history of venereal disease, the lesions of which were not properly treated. Medical advice was not sought by 58.6% until 9 mo. after the appearance of the first lesion; only 11.5% saw a physician during the first few months. None were circumcised in youth or infancy; many had phimosis with large and redundant prepuces. Analysis of data from Latin America, Asia, Africa and Europe reveals that circumcision within 8 days of birth constitutes an effective prophylaxis; that at a later date constitutes an effective guarantee against this form of cancer.

- 63-754 VITAL STATISTICS OF THE UNITED STATES 1960. VOLUME II - MORTALITY, PT. B. U. S. Dept. Health, Education, Welfare and Public Health Serv. Washington, D. C. 1963, 567 pp and index of tables. \$4.50

Of the 11 tables of mortality data for the U.S. 3 are concerned with infant and neonatal deaths, and 2 with deaths from specified infective diseases. Two tables deal with deaths by age, color and sex for the U.S. and each State for (1) metropolitan and nonmetropolitan counties, and (2) for standard metropolitan statistical areas. There are 3 tables for deaths from 59 selected causes (including 10 for well-defined malignancies): (1) by age, color, and sex, each state (2) a summary table for each state; (3) for standard metropolitan statistical areas. Table 9, which encompasses fewer diseases (but still including 8 separate categories of malignancies + "total malignancies" and "others") gives a broader geographic analysis. For each state is

ven the total incidence, followed by total rural and urban figures; then follow totals of 1 metropolitan counties and nonmetropolitan counties (each again subdivided according to urban and rural). The bulk of the table is devoted to an analysis for each county and specified urban places within that county. A separate section deals with Puerto Rico and the Virgin Islands.

-755 PRECANCEROUS LESIONS OF THE ORAL CAVITY. (Sp.) Bianchi, H. B. (Buenos Aires). Hospital (Rio de Janeiro) 4092, Buenos Aires. 1963.

analysis of 320 cases of leukoplakia observed between 1937 and 1956, 40% were among tobacco smokers, 10% could be attributed to prolonged local irritants, 8% were associated with syphilitic lesions, and the remainder were idiopathic. In a smaller series of 98 pts., age distribution: 20-30 yr., 4 and 2; 30-40 yr., 6 and 8; 40-50 yr., 16 and 10; 50-60 yr., 15 and 12; 60-70 yr., 17 and 10. No lesions were seen in pts. younger than 10 yr. In most pts., the lesions remain stationary for up to 10 yr.; but in a few pts. over 40 yr. of age, the plaque may acquire a reddish color and (eventually) a verrucous surface. These lesions may eventually ulcerate, become indurated, and be accompanied by local adenopathy. These cancers should be differentiated from the carcinomas *in situ* found on biopsy of some leukoplasias. Differential diagnosis and treatment of precancerous leukoplasias are reviewed briefly.

-756 HEPATOMA: REVIEW OF 43 CASES WITH COMMENTS ON SYPHILIS AS AN ETIOLOGIC FACTOR. (E.) Wells, R. F. (William Beaumont Hosp., El Paso, Texas) and G. D. Lundenberg. Gastroenterology 44(5):598-601, 1963.

43 Brooke Gen. Hosp. pts. with hepatomas recorded from 1948 through 1961, 15 (35%) had histories of syphilis treated by heavy metals (6/15) or had serological evidence of lues (6/15). Incidence of these findings in 1957-1961 was 10%. The interval from heavy metal therapy to diagnosis of hepatoma varied 3-37 yr. Histories of multiple inj. were not obtained for nonsyphilitic pts. except for 2 insulin-treated diabetics. Necrotic cirrhosis was the dominant form of underlying liver disease in this group (12/15 of syphilitic pts., 20/43 of the entire group). Histories of heavy alcohol ingestion were given for 9/15.

-757 EFFECTS OF DIAGNOSTIC IRRADIATION. (E.) Wise, M. E. (Inst. Radiopath., Physiol. Lab., Leiden, Holland). Lancet 1052-1053, 1963.

In answer to Dr. Burch's rejection of hypothesis A (that the excess of myeloid leukemia is due to diagnostic X-rays to the trunk) in favor of B (that most of the excess is due to lower pre-leukemic fitness of the groups receiving trunk X-rays in excess), the author states that his modal interval (time between irradiation and onset in the Oxford adult leukemia survey) was between 36 and 40 mo. The time intervals for 20 myeloids assumed to be induced by therapeutic X-rays show 2 modes at 4 and 7 yr. The evidence relating to the people who had respiratory diseases in the previous 5 yr. supports A rather than B. There is an upward trend in the relative excess of myeloids with increasing number of exposures: for 4-7, exposures, 8-15, and 16-31 exposures, the ratio of the difference between the expected number of myeloids and the actual number to the expected number was +0.656, +0.984, and +1.525, resp.

63-758 THE INCIDENCE OF MALIGNANT TUMORS IN JAPANESE CHILDREN. (E., Abstract) Takatsu, T. (U. Tokyo Sch. Med., Japan). Nippon Geka Gakkai Zasshi (J. Jap. Surg. Soc.) 64(1): 16-17, 1963.

In 1950 the death rate (per 100,000) due to malignant tumors among children aged 1-4 yr. was 5.1, and increased every yr. to 7 in 1958; for those aged 5-9 yr., increase was from 2.3 to 4.1; among those 10-14 yr., increase was from 2.5 to 3.9. The peak of incidence was between ages 2-3 yr. Incidence of brain tumor, abdominal symphaticoblastoma, Wilms' tumor and leukemia were high.

63-759 EDITORIAL. SMOKING AND HEALTH. (E.) Lancet 1:1090, 1963.

The council of the Metropolitan Borough of Chelsea has distributed to every household within its jurisdiction a booklet in which the case against smoking is presented clearly, succinctly, and authoritatively.

63-760 THE PREVENTION OF DISEASE IN MIDDLE AGE. (E.) Taylor, I. (London County Council, England). Public Health 77(4):231-236, 1963.

For men aged 50-69, the mortality from lung cancer per 100,000 man yr. was 3, for nonsmokers; 51, 59 and 144 for those smoking less than 10, 20 or 40 cigarettes/day, resp.; for those smoking more than 40/day the rate was 217. Lung cancer mortality per 100,000 man yr. was 157 for those still smoking, 78 and 60 for those who had stopped smoking for 1-10 yr. and 10 or more yr., resp., and 3 for nonsmokers. These findings suggest that efforts to modify established habits in adults should be attempted.

See also abstract nos.: 611,637

MISCELLANEOUS

- 63-761 A MODEL OF NORMAL AND MALIGNANT REPLICATION OF NUCLEIC ACIDS. (E.) Gemant, A. (Grace Hosp., Detroit, Mich.). Grace Hosp. Bull. 41(1):7-16, 1963.

Normal and malignant template replication of polynucleotides was studied by means of a physico-chemical model: the rate of crystallization of salts of certain biochemically essential compounds. Several saltlike compounds were crystallized from solutions with 2 solutes, the process being followed by the increasing optical density of the solution. In each case diagrammed, the speed of crystallization was substantially retarded by addition of small amounts of a third substance. In the case of magnesium oxalate (120 mg/100 ml and 430 mg oxalate/100 ml), which crystallized to an o.d. of 0.15 in 40 minutes, addition of 2.0 mg/100 ml of calcium reduced crystallization to an o.d. of approximately 0.06 in the same time; with 1.0 mg of Ca the rate was reduced to 0.01. Similar retardation of crystallization was obtained for urea oxalate by the presence of piperazine (though not in inverse relation to its quantity as with calcium); for crystallizing copper-uracil and mercury-adenine solutions by the presence of silver, and for crystallizing adenine oxalate by the presence of picric acid. Transferring this result to the problem of cell proliferation, it would appear that absence of certain regulator compounds necessary for maintaining a normal rate of growth may be a factor in production of malignancy. Metal cations may often be the regulator needed for normal replication rates and forms. This agrees with the deletion theories of cancer, which consider malignancy a condition where a compound needed for normal cell reproduction is lacking.

- 63-762 ON THE QUESTION OF THE MECHANISM OF GROWTH OF A TUMOUR AGAINST ISOIMMUNITY. (E.) Koldovský, P. (Inst. Exp. Biol., Acad. Sci. CSSR, Prague) and J. Svoboda. Folia Biol. (Praha) 8(2):95-100, 1962.

A 3,4-benzpyrene-induced fibrosarcoma, Bp/A (in strain A mice) after 2 serial passages through preimmunized mice gave rise to resistant tumor RBp7/A; it was then tested against preimmunized mice. As occurs with the original strain, no tumor formation followed a test inoc. with 10^4 cells; but at a dose of 10^6 cells, both strains overcame the induced immunity to form tumors in 4/10 and 3/10 challenged mice, resp. Preimmunization with each of the two strains (irradiated) in increasing doses showed tumor growth completely suppressed by 2×100 mg of Bp7/A and by 2×10 mg of RBp7/A, demonstrating a 20-fold increase in antigen in the resistant RBp7/A. In further tests of tumor growth, large preimmunizing doses of Bp7/A (100 mg) or 10 or more mg of RBp7/A had a paradoxical effect. All immunity was lost and tumors outgrew their untreated controls.

- 63-763 ON THE QUESTION OF THE ROLE OF HETEROLOGOUS TOLERANCE IN POSSIBILITY TO IMMUNIZE AGAINST TUMOUR ANTIGEN. (E.) Koldovský, P. (Inst. Exp. Biol., Acad. Sci. CSSR, Prague) and J. Svoboda. Folia Biol. (Praha) 8(2):101-104, 1962.

The growth of a benzpyrene-induced sarcoma of inbred strain A mice (Bp7/A), inoc. s.c. to 5 groups of 20 A mice each at (5×10^5 cells), was observed for 45 days. On the 1st, 3rd, and 5th day after tumor inoc., each group received 0.2 ml i.p. of a Wistar rat serum or antiserum as follows: A, antiserum from tolerant rats immunized with Bp7/A tumor; D, antiserum from tolerant rats immunized with the tumor; E, serum from normal rats. The greatest inhibitory effect on tumor growth was from tolerant rats immunized with tumor (Group D).

- 63-764 SENSITIVITY OF A TUMOUR TO IMMUNITY IN RELATION TO ITS ANTIGENICITY. (E.) Koldovsky, P. (Inst. Exp. Biol., Acad. Sci. CSSR, Prague) and J. Svoboda. Folia Biol. (Praha) 8(3):144-146, 1962.

Strain A mice, preimmunized against tumor antigen by i.p. admin. of 20 mg irradiated Bp7/A tumor, were challenged three wk. later with living tumor cells of Bp7/A or RBp7/A. No mice inoc. s.c. with Bp7/A died with tumor, but of those inoc. with RBp7/A, 2/5 died at the smallest dose (1×10^4 cells) and 5/5 died at 4×10^5 cells. Thus, the strain RBp7/A, which on repeated passage became more antigenic, also became more resistant to antitumor isoimmunity.

- 63-765 CYSTS IN MICE OF THE LOW CANCER LINE C57BL. (Rus.) Zhdanov, V. M. (Inst. Virology, Acad. Med. Sci. USSR, Moscow) and V. A. Parnes. Biull. Eksp. Biol. Med. 55(4):82-91, 1963.

Cellular cystic suspensions (from lymph nodes of mice originally subjected to a brain filtrate from a pt. who died of acute leukemia) from the 6th passage of C57BL mice and the 14th passage in random bred mice was 100% transplantable into CC57BR and CC57W mice but only through 2-3 subsequent passages of random bred mice. These 2 lines and Wistar rats developed cysts upon heterologous inoc. as well. The attempt to transplant cystic material to BALB, A, ASn, Afb, C3HA, C3HF mice and random bred rats gave negative results. The cell-free cystic suspension from passages 2, 3, and 6 in C57BL mice, inj. s.c. or i.p. into C57BL, CC57BR, CC57W and C3HA mice resulted in leukemias or tumors in 5/21, 14/37, 9/33 and 8/23 resp., and in cyst formation in 2/21, 4/37, 6/33 and 1/23, resp.; and these occurred at a more mature age compared to the effect of cellular suspensions which caused the growth of tumors and cysts in animals 18 days-4.5 mo. of age.

stic material with added brain suspension from a C57BL mouse, previously inj. with brain fil-
ate of a man who died from acute leukemia,
d induce, after 0-5 passages, cyst formation
16/43 C57BL and 24/67 CC57BR mice.

-766 DEVELOPMENT OF SARCOMAS IN THE SCARS
RESULTING FROM GUNSHOT WOUNDS. (Rus.)
slitser, L. N. (Kiev A. A. Bogomolets Med.
st. Order Red Banner Labor, Kiev) and V. V.
alik. Vop. Onkol. 9(4):95-98, 1963.

o male pts. are presented who developed sarcoma
the site of shotgun wounds in the forearm and
est 6 and 17 yr. previously, resp. In the
rst case, the process of wound healing re-
red a long period of time; this was followed
the appearance of a small tumor on the scar
ssue. Repeated surgical excision did not
rove the condition and amputation of the
rearm was deemed necessary, but the pt. died.

-767 STUDIES ON A TRANSPLANTABLE MASTOCYTO-
MA IN MICE. I. ORIGIN AND GENERAL
PHOLOGY. (E.) Rask-Nielsen, R. (U. Inst.
chem., Copenhagen) and H. E. Christensen.
Nat. Cancer Inst. 30(4):743-761, 1963.

Female (CBA x DBA/2)F₁ mouse which received
kemic tissue from a 3rd mouse passage of a
asma cell leukemia, s.c., at 4 mo. showed no
sible evidence of tumor take, either at that
ne or at autopsy, 22 mo. later. However,
autopsy, the omentum and intestinal mesentery
re filled with 2-3 mm, white, opaque nodules
sisting of mast cells with many metachromatic
d orthochromatic granules. Groups of mast
ls were also demonstrable in the liver, spleen,
ph nodes, and many other organs (especially,
the uterine wall). Successful s.c. and i.p.
nsplant of this murine mastocytoma had been
de for 2 passages, at the time of report.
avy amyloidosis was seen in most organs of the
use with the primary tumor and varying degrees
amyloid development were observed in mice
ch transplanted tumors. While amyloid formation
y occur unrelated or only unspecifically re-
ed to coexisting neoplastic growths in these
ce, other work suggests an etiologic connection
ch leukemia.

-768 OBSERVATIONS ON THE ORIGIN OF ADENO-
MATOUS EPITHELIUM OF THE COLON.
RIAL STUDIES OF MINUTE POLYPS IN FAMILIAL
YPOSIS. (E.) Lane, N. (Lab. Surg. Path.,
umbia U. Coll. Phys. Surg., New York) and R.
r. Cancer 16(6):751-764, 1963.

stological examination of human minute colonic
yps including 8 serial sections studies of
ute polyps in a case of familial polyposis
onstrate the existence of 2 separable micro-
opic types: hyperplastic and adenomatous and

the probable lack of sequential relationship
between the two. No hyperplastic polyps were
found in 2 near-total colectomy specimens removed
for familial polyposis. Adenomatous epithelium
was seen to arise de novo from normal mucosa by
a process involving gradual anatomic transition
from the germinative epithelium in the deep
portion of the colonic crypts; this deep origin
would seem to bring into harmony the high growth
potential and high mitotic activity of the
adenomatous epithelium and that mucosal level
that is normally the zone of greatest mitotic
activity.

63-769 THE CHROMOSOMES OF CULTURED HUMAN
AMNION CELLS. (E., Abstract)
Petursson, G. (Sloan-Kettering Inst. Cancer Res.,
New York). Proc. Am. Assn. Cancer Res. 4(1):52,
1963.

A comparison of karyotype analysis of the FL
"transformed" human amnion cell line and of
several human amnion lines in primary culture
for 3 weeks gave further evidence for the "malignant" nature of the first cell line. The primary culture cells showed an exact diploid number with a few exact tetraploids. The chromosomal sex agreed with the phenotypic sex of the infants in 24 cases. FL cells were heteroploid in the hypertriploid region; 78% had a chromosome number of 72-76, and 2% had numbers close to double this range. Although the human origin of the FL line is still evident from chromosomal studies, a large submetacentric "marker" chromosome was characteristic of all FL cells examined. Other abnormal chromosomes were observed, but less consistently. The number of chromosomes in each group of Patau's classification varied considerably from cell to cell, except for the large acrocentrics of Group D, whose number was 9-10/cell.

63-770 STIMULATION OF THE RETICULOENDOTHELIAL
SYSTEM AND DEVELOPMENT OF EXPERIMENTAL
MALIGNANT TUMORS. (Fr.) Halpern, B. N. (Lab.
Exptl. Med., Coll. France, Paris), G. Biozzi and
C. Stiffel. C. R. Soc. Biol. (Paris) 156(6):
1001-1005, 1962.

C₃H and Swiss mice showed no change of phagocyte activity following inoc. of J Sarcoma (developed in C57Bl mice). They developed 100% fatal tumor takes, with an av. rate of tumor growth of 1.0 and 1.4 mm/day; as contrasted to 1.7 mm/day in F₁(C57Bl6 x C₃H) mice, which also developed 100% fatal tumor takes in the presence of significant diminution of phagocyte activity. At the same time, a marked stimulation of phagocyte activity in C57Bl6 mice was accompanied by tumor regression in 40% of the animals. Stimulation of phagocyte activity in all but C57Bl6 strains, by inj. of microbial extract Wxb 3148 (400 µg, i.p. 8 days before grafting) resulted in reduction of the rate of tumor growth in all strains, and survivals of 10, 15, and 20%, resp.

63-771 CHROMOSOMAL ABNORMALITIES IN MULTIPLE MYELOMA. (E.) Lewis, F. J. W. (Southmead Hosp., Bristol), M. MacTaggart, R. S. Crow and M. R. Wills. Lancet 1:1183-1184, 1963.

Two cases of multiple myeloma are reported in which chromosomal abnormalities were detected in sternal marrow specimens. Upon analysis of the aneuploid cells, a heterogeneous range of chromosomes was found. While no characteristic pattern was found, the authors state that a range of chromosomes in excess of the normal diploid number and tending to be less than tetraploid is recognized as a feature of malignancy.

63-772 A PRELIMINARY OBSERVATION ON SPONTANEOUS DEVELOPMENT OF PAPILLOMA-LIKE GROWTH ON FEMALE EXTERNAL GENITALIA OF STRAIN 129 MICE. (E.) Kimura, T. (Mie Prefect. Med. Coll., Tsu, Japan), T. Katsuya and Y. Nishizuka. Mie Med. J. 12(1):95-101, 1962.

The incidence of papilloma-like growths on the female external genitalia in one colony of strain 129 mice was 59.8% (nuliparous, 58.3%; parous, 60.6%) compared to an incidence in mice of the same strain maintained at another laboratory of 3.5% (nuliparous, 5.9%; parous 0%). The ages of affected mice ranged from 2-21 mo.

63-773 NUCLEAR SEX OF TESTICULAR TERATOMAS. (E.) Dayan, A. D. (Bernhard Baron Inst., London Hosp., England). Brit. J. Cancer 17(1):46-49, 1962.

When nuclear sex of 37 testicular teratomas was determined, 12 were female, 22 male, and 3 mosaic. The mean 11 yr. survival for the 2 classes was 51.9% for males and 53.4% for females. It is concluded that theories of teratogenesis based on a chromosome complement assumed from the observed nuclear sex of a tumor are unjustified.

63-774 INTESTINAL METAPLASIA OF THE URINARY TRACT EPITHELIUM. (E.) Gordon, A. (Neuropath. Lab., Roy. Infirm., Edinburgh, Scotland). J. Path. Bact. 85(2):441-444, 1963.

Highly differentiated cells of intestinal type were identified in the urinary tract of 2 pts. In 1, the renal pelvis showed areas of surviving but metaplastic epithelium consisting of stratified squamous mucus-secreting cells, brush border striations, Paneth and argentaffin granules. In the other pt., the bladder was lined with mucus-secreting cells. These changes occurred in response to chronic irritation and emphasize the plasticity of the mesodermal tissues.

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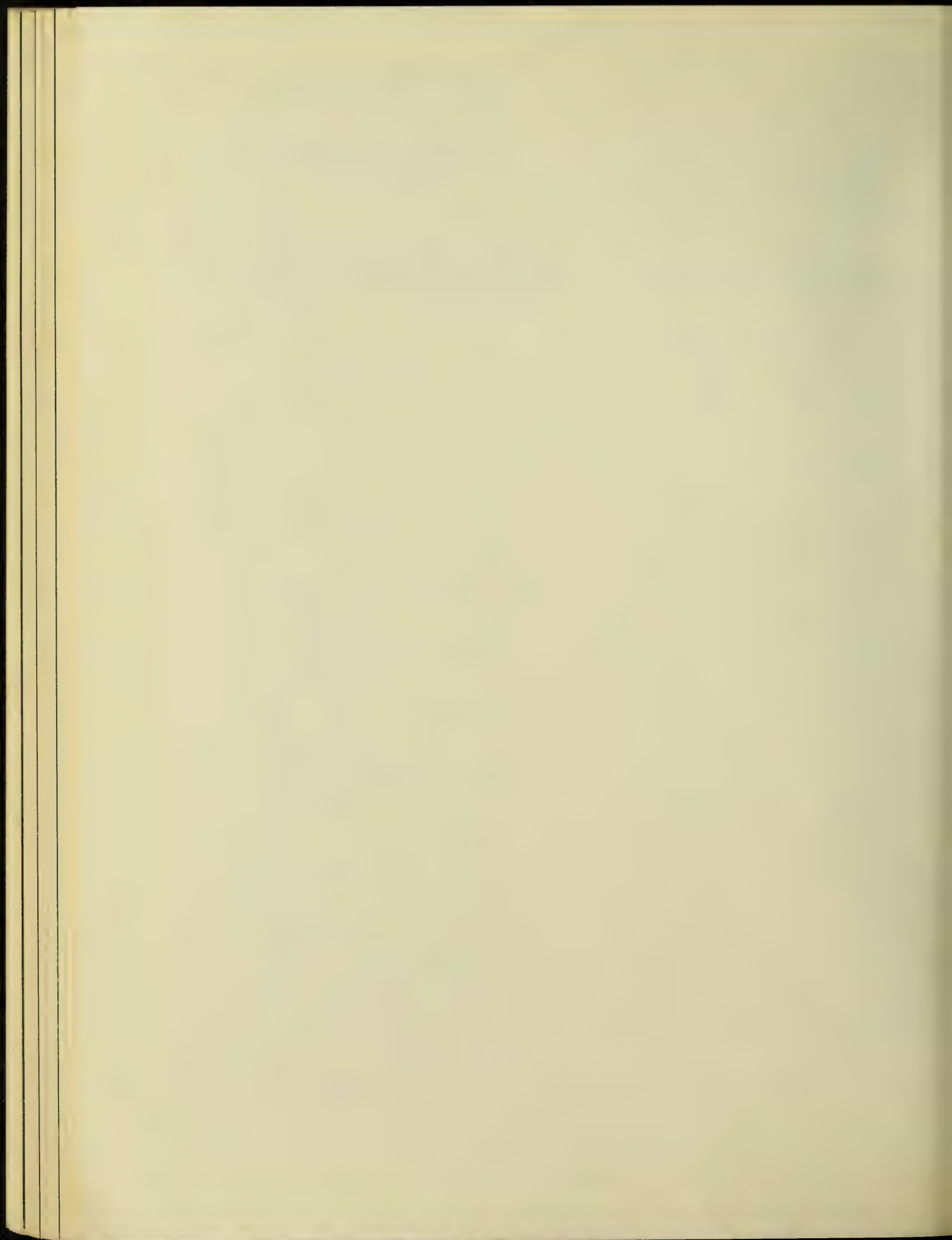
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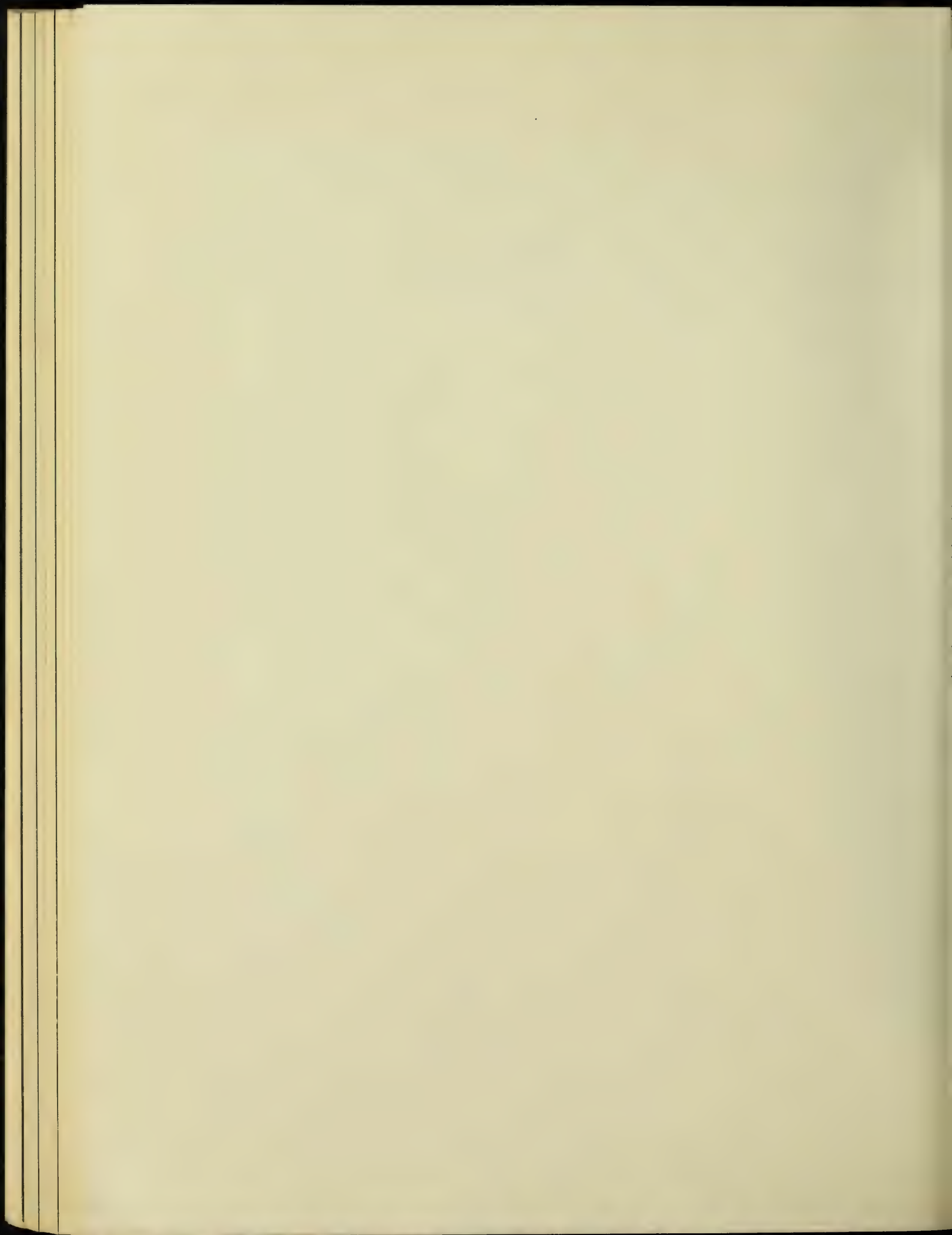
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National Cancer Institute

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Public Health Service

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health, USA
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit
e.g.	for example	ppm	parts per million
FFU	focus forming unit	pt. (s)	patient(s)
g	gram(s)	RBC	red blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
LD ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ice.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	Ind.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

775 INVESTIGATIONS ON THE BIOCHEMICAL CHARACTERISTICS AND MECHANISM OF ACTION OF ONCOGENIC VIRUSES. (Hun.) Antoni, F. Magy. Onkol. 6(4):243-247, 1962.

The author reviews the relevant findings since Pel's first observations in 1903, discussing the role of RNA- and DNA-containing viruses and their intranuclear (chromosomal and extra-chromosomal) and extranuclear mechanisms of action. He concludes that some general etiologic factor is responsible for carcinogenesis and metastasis. Investigations at the molecular level on the carcinogenic action of nucleic acids in mammalian cells can not neglect the results of observations on oncogenic viruses or the virologic approach. However, since, in the case of the malignant tumors induced by a nucleic acid preparation, it must be demonstrated that these preparations do not contain virus particles or live virus. Complex methods of investigation must be utilized, the close collaboration of oncologists, virologists, and biochemists is needed. In addition, the creation of suitable, genetically defined mouse strain cultures must be achieved. The virologic question is not only a basic problem of oncology, but also of all biological research. Its exploration with the electron microscope is urged. (No references)

76 THE DEVELOPMENT OF TUMOR VIROLOGY: POLYOMA VIRUSES AND MOUSE LEUKEMIAS. (Hun.) Vekerdi, L. Magy. Onkol. 6(4):232-237, 1962.

The recent literature is reviewed. The overall results of a decade of tumor virus research indicate that, although a new group of agents has been added to the large family of carcinogens, some of the problems of carcinogenesis can not be approached with virologic methods, the field is even more complicated than had been suspected. Suggested research goals for the future include the investigation of some of the interrelationships of virologic problems with NK/Ly ascites and collaborative physical and biochemical studies on the conditions of nucleic acid carcinogenesis as a complement to virologic studies. (No references)

77 DATA ON THE VIRAL ETIOLOGY OF HUMAN LEUKEMOSIS. (Hun.) Sellei, C. Magy. Onkol. Inst., Budapest). Magy. Onkol. 6(4):253-256, 1962.

The author cites data from the literature and summarizes the relevant conclusions of the 1961, Rye, and East Berlin Conferences on leukemogenesis. Findings about the role of viruses in human leukemia, controversial points of view regarding pathogenesis and some therapeutic considerations are reviewed. There is general

agreement that continued research on these points is urgently needed. Research problems and perspectives are examined. (No references)

63-778 VIRAL ETIOLOGY IN RELATION TO MALIGNANT TUMORS OF THE SKIN. (Hun.) Venkei, T. Natl. Onkol. Inst., Budapest). Magy. Onkol. 6(4):251-253, 1962.

Data from the literature on virus-induced dermatologic conditions are reviewed. Among the few malignant tumors known or suspected to be of viral origin, the author cites condylomata of the penis which becomes carcinomatous; malignant tumors developing from Shope papillomata (rabbits); certain cutaneous and mucosal tumors in hares, dogs, and horses; and keratoacanthoma. (No references)

63-779 EPIDEMIOLOGY AND PREVENTION OF CANCER. (Kor.) Kwon, E. (Sch. Publ. Health, Seoul Natl. U., Korea). J. Korea Med. Assn. 6(2):151-154, 1963.

A brief discussion of various factors involved in carcinogenesis and the principles involved which can serve in prevention. Mentioned are: age, sex, genetic and environmental factors, other diseases, endocrinological and occupational factors, as well as the intake of stimulants. No statistical data is included, except that on the incidence of gastric carcinoma as found in autopsy material. (6 references)

63-780 BIOCHEMISTRY OF CANCER. (Kor.) Lee, K. B. J. Korea Med. Assn. 6(2):100-108, 1963.

A review of the biochemistry of cancer which includes a short section on precancerous tissues and the changes that occur during tumor development. (149 references)

63-781 THE MECHANISM OF TUMOR INDUCTION BY AROMATIC AMINES AND OTHER CARCINOGENS. (E.) Boyland, E. (Chester Beatty Res. Inst., London). Zschr. Krebsforsch. 65(4):378-384, 1963.

Aromatic amines (2-acetamidofluorene, 2-naphthylamine) are not direct carcinogens but are converted *in vivo* to active compounds (probably arylhydroxylamines which have chemical properties similar to those of carcinogenic alkylating agents). Most carcinogens react *in vivo* with sulfhydryl compounds--arylhydroxylamines, for instance, can give rise to S-aminophenyl derivatives. Reaction with glutathione probably leads to inactivation of the carcinogens or to detoxication. In the case of alkylating agents, for

example nitrogen mustards, epoxides and mesyl esters, like ethyl methanesulfonate and busulfan, the applied biologically active compounds are chemically reactive and probably direct carcinogens. Some active carcinogens (such as polycyclic hydrocarbons and aromatic amines), appear to be converted to chemically reactive derivatives by metabolic processes (the conversion of hydrocarbons to epoxides by the addition of O_2 , oxidation of some aromatic amines to reactive hydroxylamines). The carcinogenic hydrocarbons may possibly be oxidized to dicarboxylic acid derivatives (e.g. 1,2,5,6-dibenzanthracene converted to protein-phenylphenanthracene dicarboxylic acid derivative in mice) leading to combination with proteins and sulfhydryl compounds. The metabolic reactions with hydrocarbons are probably detoxifications; the carcinogenic effect is probably produced by complex formations with the purine bases of DNA. (22 references)

- 63-782 PARAMAGNETIC STRUCTURES IN BIOLOGY. (Fr.) Garsou, J. L. (U. Liege, Belgium). *Rev. Belg. Path.* 29(5):249-271, 1963.

Paramagnetism, the property derived from free electrons, is briefly reviewed by the authors in a discussion of the role of ionization in the biologic effect of radiation and a possible role for free electrons in the process of carcinogenesis. A direct relationship has been found between certain paramagnetic structures (p-phenylenediamine derivatives, diphenols and aminophenols) and carcinogenic action; but on a broader basis theories of mechanisms of action do not appear to correlate consistently with structural considerations, and more studies of the biologically active forms of the compounds in question are required. (80 references)

- 63-783 ENVIRONMENT AND MICROORGANISMS IN NEOPLASTIC DISEASE. (E.) Hadley, H. G. (Res. Found. Inc., 4601 Nichols Ave., Washington, D.C.). *Med. Times* 91(4):372-378, 1963.

Environmental causes do not give rise to tumors by direct action but enhance a latent preexisting condition. The environment to be responsible for neoplasms must be the source of a ubiquitous inciting agent of all types of cancer. Stomach cancer is prevalent in areas with certain soil, chrome tanneries, and water with high organic carbon. Cancer is prevalent in areas of heavy rainfall, which use river rather than well water, and in low lying lands. Geographic distribution, sex differences, and occupation are important etiologically. A high incidence of oral and pharyngeal cancer is found in Sweden and Finland where fish and reindeer are eaten which may cause the Plummer-Vinson syndrome with multiple vitamin deficiencies. Navajos appear to have very little cancer. Some types of malnutrition

give a predisposition to cancer (gastric mucosa atrophy in pernicious anemia) while overeating appears to have unfavorable influences. When the sera of 16,909 noncancer pts. and 303 cancer pts. were tested with antigen prepared against *Bacillus cereus* isolated from leaf spots of a castor bean plant the leaves of which were inj. 2 wk. previously with an emulsion of ground carcinoma tissue, positive tests were observed in 220 (0.014%) of noncancer pts. and 261 (0.86%) of cancer pts. (standard deviation 3%; odds against chance occurrence 1 to 4×10^{11}). It is concluded that the presence of immune reactions between a cancerous individual and a bacterial agent may indicate a correlative relation to an inducing factor which acts upon the organism prepared to bear the effects because of some special disposition of its genetic factors. (83 references)

- 63-784 CYTOGENETIC STUDIES IN CHRONIC MYELOID LEUKEMIA. (E.) Court Brown, W. M. (Med. Res. Council, Western Gen. Hosp., Edinburgh Scotland) and I. M. Tough. Pp. 351-381 in *Advances in Cancer Research*, Vol. 7. Haddow, A. and S. Weinhouse (Eds.). New York, Academic Press Inc., 1963.

The authors review the literature dealing with the discovery of the first human cancer (chronic myeloid leukemia) with a recognizable genetic marker. Drawing on their published and unpublished work and that of the Philadelphia group (Nowell and Hungerford) technical considerations are dealt with along with a consideration of the normal human karyotype. Employing both culture and direct technics, findings are described for blood and marrow of groups of untreated and treated pts. in different stages of the disease. Since data on the frequency of the Ph^1 chromosome is related to the number of scorable cells, and this number varies according to the quality of the preparations, frequency ranges from 0%-100%, with a mean frequency of 67.6%. With the onset of acute transformation, additional abnormal cells may appear. Certain points emerge from their studies in chronic myeloid leukemia. The Ph^1 chromosome is almost certainly derived from a member of pair 21, through deletion of material from the long arm. This chromosome has appeared in all untreated cases examined to date in which suitable preparations were available. It has been found in nearly every case seen for the first time in the chronic stage but after treatment. Negative findings are believed to be confined to pts. in good clinical remission. The significance of their findings in connection with the etiology of chronic myeloid leukemia and the problem of radiation-induced disease is discussed at some length. (25 references)

- 63-785 THE MORPHOLOGY OF ONCOGENIC VIRUSES. (Hun.) Lapis, K. *Magy. Onkol.* 6(4):247-251, 1962.

ent discoveries achieved with electron microscopy and related technics are reviewed. The three approaches considered are: (1) observations on the morphologic characteristics of the viruses themselves; (2) study of the intracellular aspect of viruses, the ultrastructural changes they cause, and the micromorphology of virus-induced tumors; and (3) the use of the electron microscope to supplement the biologic and biochemical methods commonly employed in virology. (No references)

786 ETHIONINE CARCINOGENESIS. (E.) Farber, E. (U. Pittsburgh Sch. of Med., Penn.). Pp. 383-474 in *Advances in Cancer Research*, Vol. 7. Haddow, A. and S. Weinhouse (Eds.). New York, Academic Press, 1963.

This review of the production of tumors by ethionine goes into the compound's natural occurrence, both its acute and chronic biologic effects, its metabolism (including sulfur carboxyl activation) as well as detailed discussions of the carcinogenic action, both at the cellular level and in terms of altered biochemistry. In the liver, recent work indicates that many of the acute effects may not be mediated by a direct action on the protein synthetic systems but via an indirect mechanism, possibly through ATP. A detailed table indicates the acute effects of ethionine in various whole animals, organs, tissues, embryos and fetal tissues, blood, tumors, as well as Ehrlich ascites cells in the mouse, as found by many workers. A somewhat similar table summarizes the work done on chronic effects in mammals. In connection with the carcinogenic action, effects at the cellular level are examined and compared with early effects of other carcinogenic agents. There is as yet no general agreement as to which cell or cells are first affected. Besides incorporation into protein, recent work has demonstrated that ethionine labeled in the methyl carbon of the ethyl group becomes incorporated in some fashion to liver RNA and possibly also to liver DNA. This assumes importance since the RNA labeling of other organs by comparison is insignificant compared to liver, while labeling of proteins is comparable to or greater than that in liver. (Approx. 360 references)

787 AVIAN VIRUS GROWTHS AND THEIR ETIOLOGIC AGENTS. (E.) Beard, J. W. (U. Med. Ctr., Durham, N.C.). Pp. 1-127 in *Advances in Cancer Research*, Vol. 7. Haddow, A. and S. Weinhouse (Eds.). New York, Academic Press Inc., 1963.

Included in this review of virus-induced avian neoplasms are 5 which produce fibrosarcoma (Rous, Rous-Jones Farm 4 and 11, Bland-Sutton 1, Chicken 10 and Mill Hill 1); 3 myxosarcoma (Rous

sarcoma, Fujinami sarcoma and Hayashi); 2 osteochondrosarcoma (Chicken tumor VII and Muto); 1 endothelioma (Mill Hill 2) and 1 hemorrhagic disease (Duran-Reynals). Six established lines, Strain R, Strain ES4, BAI Strain A, RPL Strain 12, Strain 13 and Rous sarcoma are examined in connection with factors which influence host response (genetic constitution, dose related responses, route of inoc., age, cumulative effects); physical, chemical, antigenic and immunologic characteristics; cell growth and virus synthesis *in vitro* (myeloblasts, erythroblasts, Rous sarcoma); ultrastructural morphology in different cells and tissues; and cytochemistry. While the high frequency of occurrence of chicken tumors conveys a great impression of number and complexity of agents, in principles of pathology, the number and types of neoplasms are surprisingly small. All are of cells of mesodermal origin and each is characterized almost entirely, but not quite so, by the potentials of growth of the cell type rather than by the virus itself. The apparent present uniformity of influence of the strains discussed is related in part to selection and in part to the standardization of the study procedures. The findings suggest that the avian tumor viruses are genetically unstable and might easily be affected by processes of adaptation and spontaneous mutation, but, in view of the variables involved, such changes would be difficult to detect. (Approx. 290 references)

63-788 . THE *IN VITRO* ANALYSIS OF MALIGNANCY INDUCED BY POLYOMA VIRUS. (E.)

Sachs, L. (Weizmann Inst. Sci., Rehovoth, Israel). *Acta Un. Int. Cancr.* 19(1-2):417-421, 1963.

The author presents a review of his work. Polyoma virus (PV) synthesis can be induced *in vitro* and in transplanted mouse tumors. Kinetic studies revealed that a large quantity of infectious PV was produced per cell and was released by a cell burst of about 1,000 PFU; this mode of virus production implies that virus producing cells die. A specific resistance was found in part of all the tumor cells even among the nonvirus producers. Inoc. of *in vitro* transformed hamster cells can result in the *in vivo* development of progressively growing tumors. Growth of readily transplantable tumors can be inhibited by inoc. of the grafted animal with PV; inhibition may be the result of antigenic changes. Lack of growth *in vitro* and *in vivo* is therefore no proof of absence of malignancy. After infection of mass cultures of normal mouse embryo cells, even at a virus:cell ratio of 530 PFU/cell, only 10% of cells became virus producers during a single cycle of virus multiplication; the remaining cells presumably responded in a nonlytic interaction that resulted in transformation. Infection of cultures with a virus:cell ratio of 940 PFU/cell resulted in 90% virus producers. Only 1% of cells were competent to be transformed. PV-induced transformation was a rapid process occurring soon after virus infection. (29 references)

- 63-789 CONSIDERATIONS ON THE ETIOLOGY OF MULTIPLE HETEROLOGOUS PRIMARY INTRACRANIAL TUMORS. REPORT OF A CASE WITH ASSOCIATED MENINGIOMA AND GLIOMA. (It.) Davini, V. (Neurosurg. Clin., U. Genoa, Italy). Minerva Neurochir. 6(2):49-53, 1962.

On the basis of a detailed case report of a 47-year-old man who died 7 days after partial excision of an astrocytoma complicated by a meningioma, the author discusses the pathogenesis of CNS tumors in general terms. After pointing out that most multiple heterologous tumors are found in males over the age 50, he reviews the literature on the etiology of CNS tumors. In view of the simultaneous occurrence of such heterologous tumors in both mesodermal and ectodermal tissue, the unicentric or dysembryogenetic theory may be difficult to maintain except on the basis of coincidence or the later growth of embryonic rests at different stages of development. The polycentric theory of the malignant transformation of normal tissue through the precancerous stage is confirmed by many experimental studies which show that factors such as hormones, chemical agents, viruses and radiation may be involved in carcinogenesis, although CNS tumors resulting from orally administered carcinogens are very rare. However, the same carcinogen, implanted locally can produce both gliomas and meningiomas (i.e. 2-acetylaminofluorene). In man, however, since no exogenous factors are recognized, dysembryogenesis is the most likely etiology of CNS tumors, the non-uniform distribution being ascribed to hormonal influences. Generally, those most likely to be dysembryogenetic in origin are, presumably, the most benign. In the case of multiple heterologous tumors, it is also possible that the first tumor may provoke the second due to proliferation of normal tissue around the first tumor, or that adult CNS cells may be dedifferentiated under the influence of toxic factors from the first tumor. (32 references)

- 63-790 NEOPLASTIC TRANSFORMATION BY POLYOMA VIRUS AND ITS WIDER IMPLICATIONS. (E.) Stoker, M. G. P. (Dept. Virol., U. Glasgow, Scotland). Brit. Med. J. 1:1305-1311, 1963.

In a review of the current knowledge concerning malignant transformation by polyoma virus, the natural distribution, nature and tumor inducing ability of the virus are discussed. Cultures of polyoma transformed hamster cells are indistinguishable from those induced *in vivo*. It is believed that neoplastic transformation *in vitro* is equivalent to the initial stage of *in vivo* tumor induction. The new properties of transformed cells are possibly due to the formation of 1 or more new proteins corresponding to the antigen found in tumor cells. The virus is believed to act directly on the transformed cell rather than indirectly through an intermediate cell. Hypothetically, the virus

acts as a mutagen, adding information to the genetic material of the cell or releasing a neoplastic potential through the removal of a repressor. (53 references)

- 63-791 IMMUNOLOGICAL TOLERANCE AND THE CANCER PROBLEM. (E.) Hasek, M. (Inst. Exp. Biol. Genetics, Czech. Acad. Sci., Prague), J. Svoboda and P. Koldovsky. Acta Un. Int. Cancr. 19(1-2):102-104, 1963.

In a brief review of current research it is mentioned that ducks inoc. repeatedly after hatching with fresh or lethally irradiated (16000 r) chicken blood (no details) developed immunological tolerance to nonviral chicken tumors (0.5 ml 50 suspension, tumor unspecified, at 4 days) with 87 and 80% of the ducks dying from the tumor. Tumors inoc. into ducks untreated with chicken blood failed to kill their hosts. Tolerance to the tumor antigen contained in the benzpyrene-induced tumor Bp7/A (0.2 ml, 1% cell suspension) was developed in antigenically homogeneous inbred adult A mice by inoc. of newborn animals with lethally irradiated tumor cells. Immunization with the same tumor cells at a later age failed to induce tolerance, and 17/20 mice remained resistant to subsequent tumor inoc. However, tolerance lasting 6 mo. or more could be induced in adult mice by increasing the amount of tumor antigen (e.g. the irradiated cells) by a factor of 4x. Tolerance may also be a factor in spontaneous occurrence of tumor growth, because evidence suggests that both chemically and virus induced tumors contain antigens different from those in normal cells. The possibility is, therefore, not excluded that the induction of tolerance to these foreign antigens is one of the conditions for initiating the tumor process (19 references)

- 63-792 IMMUNOLOGICAL FACTORS INFLUENCING POLYOMA VIRUS ONCOGENESIS. (E.) Habel, K. (NIH, Bethesda). Acta Un. Int. Cancr. 19(1-2):113-114, 1963.

A brief review of the work detailed in CRA 1(3) #508, 1963. (6 references)

- 63-793 POLYOMA VIRUS CARCINOGENESIS. (E.) Stewart, S. E. (NIH, Bethesda). Acta Un. Int. Cancr. 19(1-2):255-262, 1963.

The discovery and some of the characteristics of polyoma virus carcinogenesis are reviewed. Mammalian tumor viruses are classified into those which are intracytoplasmic--fail to incite antibody response, and appear not to spread by contact (such as the mammary tumor and the various leukemia viruses, with the exception of Friend's leukemia); and those which are intranuclear--produce antibodies in the infected host, and do not cause spontaneous tumors in their natural hosts, such as polyoma, SV40, and probably

novirus type 12. Of tumor viruses, polyoma the most antigenic, producing antibodies in infected animals demonstrable by inhibition of or induction, and also by hemagglutination inhibition. The Shope papilloma virus, also a cytoplasmic, highly antigenic virus, produces benign tumors in the cottontail rabbit which is its natural host, and benign tumors transforming into adenocarcinomas in the domestic bit. Among intracytoplasmic viruses, the Rous sarcoma virus appears to be hormone dependent, whereas most of the mouse leukemia and the fowl leukemia viruses do not depend on any known factor for initiating malignant transformation. The polyoma virus has a dual effect both in vivo and in tissue culture: production of cell proliferation and also destruction of infected cells. The last effect was used by the author to demonstrate that virus from tumors derived from monolayer plaques caused similar incidences of 11 types of tumors in mice, indicating that a single virus was involved. Although many tumor viruses are recoverable at an early stage of development and not at other stages (e.g. the Shope papilloma virus and the Rous sarcoma virus) attempts at demonstration of a single virus have so far been unsuccessful. (17 references)

794 INAPPARENT TRANSMISSIBLE AGENTS IN ONCOLOGY AND THEIR INFLUENCE ON TUMOR HOST. (E.) Riley, V. (Sloan-Kettering Inst., Rye, N. Y.), E. Huerto, J. D. Loveless, J. Bardell, M. Fitzmaurice and C. Forman. Un. Int. Cancr. 19(1-2):263-270, 1963.

For detection, properties, and some of the secondary biological and biochemical effects of transmissible particle(s) associated with mice bearing a variety of transplanted tumors are reviewed. If plasma or tissue extract from a tumor bearing any one of some 35 transplantable plasmas are inj. into normal healthy mice there is a 5-10-fold increase in plasma lactic dehydrogenase (LDH) activity within 48 hr., and elevating activity may be serially transferred at any time from a few minutes after inj. to the death of the inj. animal. The plasma LDH response shows some conc. dependence on number of infectious units, and no elevation is observed with less than 10^{10} infectious units. Studies of time course of the infection it appears that peak agent titer is at 36 hr., followed by 36 hr. peak elevation in plasma LDH activity (to about 5000 U). However, on tumor transplantation there is a second higher agent and peak at approx. 24 days, or when tumor volume approx. 1/2 its final volume. This very high LDH (40,000 U) and agent peak is in addition to the smaller peak observed when agent is inj. and is followed by titer and LDH decline. The same picture was obtained when tumor-free agent was inoc. into a mouse bearing an agent-free tumor (a transplantable radiation-induced pituitary tumor). Controls bearing tumor only showed little LDH elevation.

Other factors reviewed briefly are the agent-associated anemia, and effect of the agent on tumor respiration and anaerobic glycolysis. (See also CRA 1(4):#720, 1963.) (25 references)

63-795 SYSTEMIC AND LOCAL FACTORS AFFECTING GROWTH OF METASTASES IN THE LIVER.

(E.) Fisher, B. (Pittsburgh, Pa.) and E. R. Fisher. Pp. 749-765 in Biological Interactions in Normal and Neoplastic Growth. Brennan, M. J. and W. L. Simpson (Eds.). Boston, Little, Brown and Co., 1962.

In a general review of their own previously published work and that of others, the authors discuss the inhibitory effect of heparin, fibrinolysin or hypophysectomy on the development of hepatic metastases following intraportal inoc. of Walker carcinoma in rats, as well as a number of factors which seem to increase such metastasis. Various types of surgical trauma, including partial hepatectomy, laparotomy with manipulation of the liver, partial occlusion of the inferior vena cava or interruption of the arterial blood supply before or after inoc. all increased metastasis, as did stimulation by proferin or admin. of agents which block the RES such as Thorotrast and India ink; the latter induce swelling of the Kupffer cells with sinusoidal compression. Metastasis is also favored by admin. of a choline-free high-fat diet, or of a high-protein diet following inoc. of the tumor cells, as well as by admin. of pituitary homogenate. These results indicate that metastasis is, in large part, dependent upon the establishment of a tumor thrombus, and is augmented by factors which enhance the trapping of tumor cells within an organ. Tumor cells may remain dormant in parenchymal tissue for variable periods, being subsequently stimulated to growth, and hormonal factors may well play a regulatory role in this process. (33 references)

63-796 EXPERIMENTAL MAMMARY CANCER: INDUCTION AND EXTINCTION. (E.) Huggins, C. (Ben May Lab. Cancer Res., U. Chicago, Ill.). Acta Un. Int. Cancr. 18(6):973-975, 1962.

The method used for rapid induction of mammary cancer in female Sprague-Dawley rats is reviewed briefly (single feeding of 20 mg of 9,10-dimethyl-1,2-benzanthracene in oil, or single i.v. or i.p. inj.). Analysis of carcinogenic hydrocarbons indicates that certain groups are of the highest significance in producing mammary cancers (methyl, amino, or methoxy groups, or an extra ring at a salient locus), all sharing as a common factor, single electron transfer and the production of hyperconjugated aromatic molecules permitting charge transfer. In addition, carcinogenicity depends on a steric factor, and the degree of carcinogenicity increases the closer the resemblance of a polycyclic hydrocarbon has to the purine-pyrimidine base pair in nucleic acids. The observation suggests that cancers result upon specific damage to the host DNA.

- 63-797 MEDICAL ASPECTS OF SMOKING. (E.)
Wallner, L. J. (Presbyterian-St. Luke's
Hosp., Chicago). *Trans. Amer. Acad. Ophthalm.
Otolaryng.* 67(3):281-291, 1963.

A review of the literature and the conclusions of a number of health agencies indicate that cigarette smoking increases the risk of carcinoma of the lung, as well as cardiovascular disease and respiratory disease. Chemical analysis and clinical experience indicate that tobacco smoke is an irritant to the respiratory mucosa, and clinical experience shows that in heavy smokers there is chronic nonspecific inflammation of the mouth, tongue, pharynx, and larynx. Moreover leukoplakia of the mouth, tongue, palate and larynx, which is considered the result of smoking, is believed to be a common precursor of cancer. The author's studies indicating that polypoid degeneration of the vocal cords results from the irritation of cigarette smoke are also reviewed. The condition appears to be reversible when smoking is stopped. (25 references)

- 63-798 1962 REPORT OF THE SCIENTIFIC DIRECTOR.
(E.) Little, C. C. *Tobacco Indust.
Res. Comm.*: 5-58 pp., 1962.

A brief outline of the fields of inquiry covered by research projects currently sponsored by the Tobacco Industry Research Committee is followed by abstracts of papers from various publications, describing the recent findings of the grantees and the present status of their research. Included are cell and tissue culture studies, pulmonary and cardiovascular studies, tobacco biochemistry and pharmacology, and psycho-physiologic studies, all correlated to some degree with tobacco smoke and its use by man. It is emphasized that there is as yet too little real knowledge about cancer and heart disease to attribute a direct causative role to any specific factor in their origin, or to assign relative weights to individual contributing factors. A list of grantees and the titles of their projects is appended.

- 63-799 MAFFUCCI'S SYNDROME WITH TRANSITION INTO
CHONDROSARCOMA. (Rus.) Rabinovich, I. I.
(Centr. Res. Inst. Traumatol. Orthoped., Moscow)
and A. A. Arenberg. *Khirurgiia* 39(5):51-56, 1963.

In a review of Soviet and foreign literature, 54 cases of Maffucci's syndrome were found, 9 of which developed chondrosarcoma. To these the authors add 2 personal cases, both females, ages 27 and 38, both of whom developed chondrosarcoma (talus and femoral condyle, resp.). The younger pt. had metastases to the lungs, brain and kidneys. In the review series of 56, age ranged from 4.5-60 yr. with normal sex distribution. Typical signs of the syndrome include bilateral hemangiomas, phlebitis and skeletal deformities. The onset of regional pain and swelling accompany the malignant change leading to bone destruction. (No references)

- 63-800 PRECANCERS AND PSEUDOCANCERS. (Ger.)
Gotttron, H. A. (7 Watford St., Mainz,
Germany). *Derm. Wschr.* 147(14):338-344, 1963.

A review of the importance of dermatology in the study of carcinogenesis includes a discussion of the histological bases for differentiating between cancer and precancerous conditions. After emphasizing the importance of the mesenchymal substrate, alterations which affect the nutrition of the epithelial cell, there are discussions of some of the changes which characterize malignant cell change, including nuclear enlargement and variability, nucleolar hypertrophy, increased and atypical mitoses, increases in RNA in the rapidly proliferating cell layer, and changes in cellular respiration. Among precancerous conditions (the definition of which depends on the statistical fate of pts. suffering from them), the author includes dermatoses produced by X-ray, UV light and arsenic (all after prolonged exposure to low doses), as well as hereditary disruptions of the functional defense mechanisms to exogenous stimuli (e.g. xeroderma pigmentosum, kraurosis, congenital phimosis). The differential diagnosis between cancerous and precancerous conditions is discussed, with special attention to the erythroplasias. Finally, the concept of pseudocancers and pseudosarcomas is briefly outlined, the distinguishing characteristic being benign infiltrating growth such as in papillomatosis cutis carcinoides or connective tissue proliferation due to inflammation. (No references)

- 63-801 CANCER PREVENTION. (Ger.) Kretz, J.
(11 University St., Vienna). *Krebsarzt*
18(1-2):1-13, 1963.

In a review, the author discusses the concept of the cancer cell as a cell which has reverted to a more primitive glycolytic mode of catabolism, as a result of which its growth and reproduction become uncontrollable and its offspring spread throughout the body via the blood and lymph. Carcinogenesis is thus the gradual poisoning of the oxidative enzymes, leading to an irreversible and inheritable alteration in cell metabolism and eventually, through the precancerous stage, invasive growth. This process can be initiated a variety of carcinogenic agents, including radiation, coal tar derivatives in the air and food, and a variety of industrial chemicals. Emphasis is placed, however, on individual variability and the concept of the long latent period during which precancerous changes may be found in the organs most commonly affected by malignancies. In evaluating the reality of the apparent increase in respiratory cancer in men, breast cancer in women and cancer of the urinary tract in both sexes, the author takes into consideration the age distribution of the population and improved diagnostic facilities, but concludes that the increases are real. Cancer prevention, which can now be placed on a firm scientific basis, must include the avoidance of known carcinogenic

ctors such as air pollution, tobacco smoking and food additives or contaminants, good general hygiene, the maintenance of a sufficiently high level of oxygenation throughout the body, and the early recognition and treatment of pre-cancerous conditions. (No references)

802 CONSIDERATION OF MEANS FOR DETERMINING IF VIRUSES ARE CAUSALLY RELATED TO CANCER IN MAN. (E.) Moore, A. E. (Sloan-Kettering Inst. Cancer Res., New York). Pp. 5-306 in *Progress in Medical Virology*, Vol. 5. Burger, E. and J. L. Melnick (Eds.). 29 Figs. and 10 Tables. Hafner Publishing Co., Inc., New York, 1963.

Studies attempting to relate viruses to human cancers are reviewed and discussed briefly, including electron microscopic tissue and organ culture, and animal inoc. studies. The last approach has allowed detection in cell-free filtrates from tissue cultures and homogenates of human tumors of a number of agents which were non-tumorigenic when inoc. into newborn mice. In a typical experiment, after inoc. of 5000 hapazardly bred newborn Swiss mice with cell-free filtrates from human lymphomas, the frequency of tumors (mostly typical murine mammary adenocarcinomas and lymphosarcomas) after 1 yr. was raised from 4.3% in uninoculated controls to 10.2%. Material from other human tumors did not affect the frequency of murine tumors. (59 references)

803 TRANSMISSIBLE AGENTS AND ANEMIA OF MOUSE CANCER. (E.) Riley, V. (Sloan-Kettering Inst. Cancer Res., New York). *Y. Med. J.* 63(10):1523-1531, 1963.

The physiochemical characteristics, agent-enzyme-tumor interrelationships, and distribution of the lactic dehydrogenase elevating agent (LDH-elevating agent) found in a variety of transplantable tumors is reviewed (see also CRA 1(3):#345, *ibid.*, (5):#919, 1963). A possible source of plasma LDH could be in the destruction of RBC. Mice with LDH-elevating agent and Ehrlich ascites cells, there was complete agreement between increase in plasma LDH and decrease in RBC days 1-6 after inoc. At that time plasma enzyme activity had increased from 5×10^2 to 5×10^3 units, while the hematocrit had dropped from about 49% to 25%. Such an effect of plasma LDH and hematocrit may be mimicked, to a lesser extent by infection of rodents with members of the Bartonella family, such as *Erythrozoon coccoides*, although in this case plasma LDH returns to normal if the animal survives the *E. coccoides*-induced anemia crisis. A possible infection of mice caused a synergistic effect on both plasma LDH and the anemia. A direct effect of the agent on the erythropoietic system of hosts could be demonstrated by inj. of cell-free plasma from mice bearing Ehrlich's carcinoma + LDH-elevating agent in splenectomized

or X-irradiated mice. Determinations of plasma LDH in splenectomized mice gave the usual picture observed in the presence of tumor and agent. In other experiments admin. to mice of the erythrolytic agent phenylhydrazine caused a dose-related plasma LDH elevation with a concomitant dose-related anemia. Although these data indicate that the major source of plasma LDH in agent-infected hosts is RBC destruction, other sources of LDH (possibly from tumor) appear to be operative, since in sham-splenectomized animals the anemia observed after agent inj. was transient, and similar to that observed in agent-free controls, whereas the plasma LDH elevation paralleled that observed in splenectomized, agent-inj. mice. Moreover, studies of a mouse bearing a rapidly growing ascites leukemia showed, within 2 wk., a 1000-fold plasma LDH elevation, with only moderate accompanying anemia. In apparent contradiction to these data is the observation that upon irradiation with 400 r agent-bearing Swiss HA/ICR mice showed less destruction of RBC than agent-free controls, although the observation that reticulocytes recover from irradiation more rapidly in agent-infected than in agent-free controls suggests that perhaps a mild attack by the agent on some elements of the host's hematopoietic system may stimulate an earlier recovery response, which would anticipate the delayed anemia obtained in X-irradiated, agent-free animals. (19 references)

63-804 RELATIONSHIPS BETWEEN TUMORS OF THE KIDNEY AND ENDOCRINE GLANDS. (Fr.) Sorrentino, M. (Urol. Clin., U. Naples, Italy) and F. Sorrentino. *Gaz. Med. Franc.* 70(7):1191-1195, 1963.

In a general discussion and review, the authors agree that hyperadrenocorticism may favor (rather than cause) development of renal tumors and/or metastases. However, they feel that insufficient weight has been given to the existence of a renal hormone which is said to stimulate the production of aldosterone and (possibly) of all adrenocortical hormones, thus suggesting that, at least in some cases, concurrent hyperadrenocorticism may be merely a symptom of renal cancer, secondary to increased production of the renal hormone in question. It is also suggested that this, or another, renal hormone may induce a state of endocrine dysfunction in the presence of renal neoplasms which closely resembles hyperparathyroidism and which thus favors osseous metastases. (No references)

63-805 THE CLINICAL AND PATHOLOGICAL CHARACTERISTICS OF THE AVIAN LEUCOSIS COMPLEX, WITH SPECIAL REFERENCE TO ROUS AND ALLIED TUMOURS. (E.) Campbell, J. G. (Agric. Res. Coun. Poultry Res. Ctr., Edinburgh, Scotland). *Proc. Roy. Soc. Med.* 56(4):305-307, 1963.

The three major constituents of the fowl leukosis

complex, erythroleukosis, myeloid leukosis, and lymphoid leukosis are described, together with associated conditions classified as fowl paralysis, osteopetrosis, fibrosarcomas, and hemangiomas. In a discussion the author defines differences in viewpoint between British and U.S. investigators on the classification of these conditions. It is pointed out that certain criticisms can be levelled against the findings of U.S. workers, based primarily on the presence of endogenous viruses in experimental material. Working with several "lymphoid" tumors from field cases, the author and his associates have failed to observe any conditions other than the one to be expected in their inoc. birds. No classical leukoses have been observed in osteopetrosis-inj. birds in the author's closed flock of inbred Brown Leghorns almost completely free from leukosis (but not from fowl paralysis). Another criticism of much published work is that it is mainly confined to a few long-established laboratory strains, which are known to have become altered in antigenic properties (Rous sarcoma), and transmittability (the leukosis agents are egg transmitted, Rous sarcoma is not); also field cases are never epidemic. (No references)

63-806 POLYOMA AND OTHER INDIGENOUS MOUSE VIRUSES. (E.) Rowe, W. P. (NIH, Bethesda), J. W. Hartley and R. J. Heubner. Lab. Anim. Care 13(2):166-175, 1963.

In a discussion of possible approaches to control of multiple viral infections in laboratory animals, the author presents data on incidence of polyoma, K-virus, mouse adenovirus, and Reo-2 virus antibodies in laboratory, production, and wild colonies. Mouse salivary gland and thymic agent virus (assayed by direct virus isolation) are also analyzed for incidence in various populations. It is concluded that the remarkable freedom of SPF and germ-free animal colonies from all but

the Reo-2 virus strongly indicates that these populations are the only possible approach to the study of viral infections. Examples of misleading conclusions from results obtained in the presence of contaminated systems are given. Other laboratory conditions leading to contamination of animal colonies are also discussed. (21 references)

63-807 ETIOLOGY OF LEUKEMIAS. (Fr.) Bernard J. (Inst. Leukemic Res., Fac. Med., Saint-Louis Hosp., Paris). Rev. Prat. 13(16): 1959-1967, 1963.

See CRA 1(4):#608, 1963. (14 references)

63-808 HISTORICAL REVIEW AND RESEARCH PERSPECTIVES OF HORMONES IN CANCER. (Fr.) Copelman, L.-S. Canad. J. Publ. Health 54(6):91-96, 1963.

After a few brief introductory comments on the long held belief that sexual hormones and cancer of the genital glands are interrelated, the author reviews his work on the effect of gonadotropic hormones. Over 25 yr. ago the author demonstrated that gonadotropic hormones injected in puberal rats (1000-1200 U total dose) caused specific histologic alterations and hyperplasia of the zona fasciculata of the adrenal cortex. These changes were comparable to those obtained by M. Arnon after inj. of a 95% ethanol precipitates of urines from cancer pts., suggesting that gonadotropin is secreted by the cancer pt. This work is now evaluated in the context of more modern studies of adrenalectomy and castration in the treatment of mammary cancers. (5 references)

PHYSICAL CARCINOGENESIS

3-809 CANCER: RELATION OF PRENATAL RADIATION TO DEVELOPMENT OF THE DISEASE IN CHILDHOOD. (E.) Sternglass, E. J. Westinghouse Res. Lab., Pittsburgh, Pa.). *Science* 140:1102-1104, 1963.

Experimental evidence indicating a linear response and the absence of a threshold for the development of childhood cancer and leukemia at total doses below 1 r is contained in recent studies of prenatal diagnostic X-ray exposure by B. McMahon and the earlier work of A. Stewart. McMahon's study consisted of those children born between 1947-54 in New York-New England maternity hospitals who died of cancer by 1959. Among 556 single births where adequate records were found, av. cancer mortality was about 40% higher for children X-rayed in utero than those who were not; the rate was also higher for those irradiated during the first 6 mo. than the last 3 mo. A 1% increase in mortality for each 17 mr admin. to the embryo in the range investigated was found. Normal background radiation (75-150 mr in 9 mo.) may trigger 10% of all childhood cancer and leukemia. Nuclear explosions totalling 100 megatons may expose the bone marrow to 150-300 mr in 9 mo., which could increase the childhood cancer mortality for children born within the yr. after such explosions 2.5-10%. Short-lived isotopes (^{89}Sr , ^{140}Ba , ^{131}I) which comprise 75% of the activity of such explosions may be responsible for childhood leukemia since the embryonic thyroid accumulates ^{131}I at a conc. 2-10 x that of the normal adult thyroid at the end of the first trimester.

3-810 CHROMOSOMAL PATTERNS OF IRRADIATED LEUKEMIC AND NONLEUKEMIC C57BL/6J MICE. (E.) Nadler, C. F. (Dept. Med., Northwestern U. School of Med., Chicago). *J. Nat. Cancer Inst.* 25:923-931, 1963.

Chromosomes of 17 C57BL/6J female mice which received 600 r total body irradiation at 5-6 wk. were analyzed at 6-7 mo. Of 7/17 which developed leukemia, mouse #1 with generalized leukemia had 15 cells with a mode of 40, variation above the mode, and a large marker chromosome. Mouse #2 with localized thymic leukemia, had 2 hyperdiploid modes of 41 and 42 in thymic tissue, and normal chromosomes in spleen and marrow. Mouse #3 with generalized leukemia, had modes of 40 and 41 in thymus, spleen and marrow, and mouse #4, with localized thymic leukemia, had a mode of 41 with variation about the mode. Among nonleukemic irradiated mice, 1 had some cells with a pseudodiploid karyotype containing a minute chromosome, and 1 had a questionable abnormality consisting of increased variation about the mode. Normal mice had a modal diploid number of 40 with a small number of hypodiploid cells. It is not clear whether aneuploidy in irradiated nonleukemic mice may be the result of leukemic or persistent X-ray induced aberrations.

63-811 PRIMARY ATYPICAL EPITHELIAL HYPERPLASIA OF MOUSE SKIN FOLLOWING SINGLE EXPOSURES TO PROTONS, DEUTERONS AND ALPHA PARTICLES. (E., Abstract) Lippincott, S. W. (Dept. Path., Bowman-Gray Sch. Med., Winston-Salem, N.C.), J. E. Jessep, C. P. Baker, W. G. Calvo, C. R. Jansen, K. R. Rai and W. Alcober. *Proc. Am. Assn. Cancer Res.* 4(1):39, 1963.

Bombardment of mouse epidermis with accelerator-produced monoenergetic, heavy, ionizing particles (10 Mev protons, 20 Mev deuterons, or 40 Mev alpha particles) caused within 20 days, atypical epithelial hyperplasia without underlying vascular or collagen alterations. In some cases the epidermal lesions resulting from an exposure to 2000 rad resembled the skin carcinoma in situ observed in humans.

63-812 SOME RESULTS OF STUDIES ON THE NEOPLASTIC EFFECT OF RADIOISOTOPES. (Rus.) Strel'tsova, V. N. (Acad. Med. Sci., Moscow). *Vop. Onkol.* 9(3):32-39, 1963.

The neoplastic effect of radioisotopes, admin. p.o. or parenterally in supra- or threshold doses, was studied in experimental animals. ^{90}Sr , ^{89}Sr , mixture of ^{90}Sr + ^{89}Sr , ^{140}Ba , ^{239}Pu , ^{90}Y , ^{91}Y , solutions in which U was undergoing fission, ^{144}Ce , ^{137}Cs , ^{147}Pm , ^{140}La , ^{95}Nb , and ^{106}Ru produced osteosarcoma in 314/2942, and other tumors (including leukemias), in 459/2942 rats. In dogs the following tumors resulted: ^{90}Sr + ^{89}Sr , osteosarcoma in 1/4 and leukemia in 1/4; ^{239}Pu , chondroma in 1/4 and leukemia in 1/4; ^{144}Ce , leukemia in 3/18 and other tumors in 4/18. In rabbits ^{144}Ce produced osteosarcoma in 2/23 and other tumors in 2/23. In rabbits a mixture of ^{89}Sr + ^{90}Sr produced osteosarcomas in 17/58, and other tumors in 12/78. The charts representing the summary of experimental material, dosages and method of admin., latent periods, and the av. number of sarcomatous nodes/animal are included in the report.

63-813 THYROID NEOPLASMS IN SHEEP FED RADIO-IODINE. (E.) Marks, S. (Hanford Lab., General Electric Co., Richland, Washington) and L. K. Bustad. *J. Nat. Cancer Inst.* 30(4):661-673, 1963.

Admin. of ^{131}I induced multiple thyroid adenomas in 3/4 Suffolk ewes fed 1.5 $\mu\text{C/day}$ p.o. x 60-91 mo. from the time of birth plus unspecified doses from the dam from the time of conception. The 4th ewe developed a follicular carcinoma. Multiple adenomas also developed in 6/9 receiving 5 $\mu\text{C/day}$ x 68-84 mo. under similar conditions; a single, minute adenoma developed in 1; and a fibrosarcoma in 1, with 1 proving resistant. In animals receiving 45 $\mu\text{C/day}$ x 12 mo., beginning at age 15 mo., multiple adenomas developed in 2/2. Single adenomas developed in 2/4 receiving 135 $\mu\text{C/day}$ x 9 mo., beginning at age 15 mo., and 2/4 proved resistant. (Previously reported in the literature

were 5/9 receiving 5 $\mu\text{C/day}$.) The authors comment that the diet employed to achieve maximal uptake of ^{131}I may have been a carcinogenic factor, per se, being low (but marginally adequate) in stable iodine. In animals receiving 135 $\mu\text{C/day}$, maximum total radiation to the thyroid was $>100,000$ rads. It was 7,000-10,000 rads in those receiving 1.5 $\mu\text{C/day}$ and 20,000-70,000 rads in the remainder. Thyroid adenomas were not found in 22 controls and in 13 animals receiving 0.15 $\mu\text{C/day}$. However, thyroid adenomas identical to those described above were found in 2 controls and 1 sheep receiving 0.15 $\mu\text{C/day}$ aged 10 yr. or over. Age of experimental tumor appearance was 4-8 yr.

- 63-814 LIGHT-INDUCED CHEILITIS AS A PRE-CANCEROUS STATE. (Hun.) Szodoray, L. (Dermat. Dept., U. Med. Sch., Debrecen, Hungary). *Magy. Onkol.* 7(1):20-24, 1963.

Of 4522 dermatologic outpatients seen in a 6-month period, 243 had skin lesions caused by undue exposure to sunlight and 15 (12 males, 3 females) had cheilitis of the lower lip. Histologic studies on 7/15 cases of cheilitis showed precancerous changes (heterotopic proliferation of the epidermis with keratin pearls in the majority, with more or less pronounced atypia of the epidermal cells). In addition, 14 cases of cancer of the lower lip (11 men, 3 women) were observed in this series. The findings suggest that, in addition to smoking, prolonged exposure to sunlight is a significant factor in the development of cancer of the lower lip. The importance of histological investigation and prophylactic treatment is therefore apparent.

- 63-815 STUDY OF GASTROINTESTINAL TUMORS INDUCED BY RADIOACTIVE CERIUM (Ce^{144}). (Rus.) Lebedeva, G. A. *Ark. Pat.* 25(5):40-45, 1963.

Admin. of Ce^{144} (9-18 $\mu\text{C/g}$) by gastric intubation to 300 white rats led to inflammation of the g.i. mucous membranes, the severity of which varied from individual to individual and also according to dose. During a period ranging from 250-485 days after the beginning of the experiment, histological studies revealed adenomas, papillomas, leiomyomas, sarcomas as well as glandular, diffuse, mucous and solid cancer. The greatest

number of precancerous lesions occurred in the large intestine; this was evidently caused by a more intense irradiation of this portion of the digestive tract.

- 63-816 INFLUENCE OF URETHANE ON SUBCUTANEOUS CARCINOGENESIS BY "TEFLON" IMPLANTS. (E.) Tomatis, L. (Div. Oncol., Chicago Sch. Med., Ill.) and P. Shubik. *Nature (London)* 198:600-601, 1963.

In female Swiss mice implanted with Teflon (12 x 12 x 1.2 mm s.c.) at 7-9 wk., addition of urethan (0.1% in drinking water), starting 35 wk. later, increased the frequency of sarcomas at the implant site from 12.5% of 80 in controls to 24.4% of 54 mice, without affecting significantly the mean time of tumor appearance (61.6 wk. in experimental, 54.5 wk. in controls). Attempts at a better definition of the enhancing effect of urethan on sarcoma formation were made by admin. urethan earlier, starting at 15 and 25 wk. from Teflon implantation. However, mortality was extremely high in the 15 and 25 wk. treatment groups with only 2/56 and 12/57 animals surviving at 60 wk.; consequently tumor frequency was reduced to 5.2% and 10.0%, resp.

- 63-817 INHIBITION OF URETHAN LUNG TUMOR INDUCTION IN MICE BY TOTAL BODY X IRRADIATION. (E., Abstract) Foley, W. A. (U.S. Naval Radiol. Defense Lab., San Francisco, Calif. and L. J. Cole. *Fed. Proc.* 22(2):580, 1963.

Urethan (U; 1 mg/g i.p.) produced multiple pulmonary adenomas (av. 5.6/mouse) in 100% of adult C57L x A Fl hybrid mice by 24 wk. after inj. When the same U dose was inj. 1 wk., 24 hr., or 3 hr. before X-irradiation (880 rad) tumors developed in 8/15 (av. 1.5 tumors/mouse) in 2/15 (av. 1 tumor/mouse) and in 2/15 (av. 1 tumor/mouse) resp. In another group irradiated 3 hr. before U inj., 3/15 mice had tumors (1.3/mouse) at 24 wk. Normal untreated controls showed no pulmonary tumors at 24 wk., and untreated irradiated controls showed a single lung tumor nodule in 1/10 animals. The data suggest that U lung carcinogenesis may be interfered with by a direct inhibitory effect of the radiation on cells already altered by U, or through latent radiation inhibition of lung cell proliferative capacity.

See also abstract nos.: 782, 859, 878, 881, 891, 963

CHEMICAL CARCINOGENESIS

8-818 ON THE CARCINOGENICITY OF DULCIN.
(Jap., Abstract) Ikeda, Y. (Nat'l.
Inst. Hygiene, Japan). Folia Pharmacol.
58(3):44P-45P, 1962.

A group of 95 Wistar rats (including controls) fed Dulcin (0.001-1.0% in the diet for 18 mo.) had tumors were found in liver, kidney, spleen and heart. In those given more than 0.5% some histological changes were noted. There was slight inhibition of body growth and a slight shortening of life-span. The results are different from a study by Fitzhugh for U.S.A. Food and Drug Admin. in 1951 in which hepatic tumors were found. The discrepancy was thought to be due to differences in strains and evaluation time.

8-819 BIOCHEMICAL STUDIES OF RATS WITH CARCINOMA. (Jap.) Sato, H. (Dept. Med., Kagoshima U., Japan), K. Yuki, Otsuji, T. Azuma, S. Oyama, M. Moriyama, Ichiki, T. Samejima, T. Maeda, S. Maeda, Misaka, Y. Hayashi, K. Arima and M. Tokikawa. Jap. Soc. Intern. Med. 51(4):430-432, 1962.

The relationship between metabolism of blood proteins and carcinogenesis was studied in rats fed dimethylaminoazobenzene (DAB). WBC, Hb and hematocrit started to decrease soon after DAB was fed and showed minimal levels at the 4th or 5th wk. after start of treatment, followed by temporary recovery which was interrupted by the growth of the liver tumor. Catalase in the liver was decreased immediately after DAB was initiated and at the 4th wk. minimal levels were reached followed by temporary recovery between 8-12; level was again sharply decreased as the tumor developed. Apparently there was a disturbance of blood protein metabolism before the start of tumor growth. Urine urobilinogen was elevated in DAB-fed rats; S-amino levulinic acid dehydrogenase in the liver, kidney and spleen was decreased by the 6th wk. of treatment and showed a transient elevation followed by a marked decrease as the tumor developed. Tissue fractions of ferritin and hemosiderin were elevated soon after initiation of treatment but decreased as the tumor developed, whereas Fe in the spleen continued to increase. Tissue and serum Cu in the liver also showed temporary elevation followed by a decrease coincident with tumor growth. RNA in the liver, kidney and spleen was gradually elevated after treatment was started but increased significantly as the tumor developed; DNA showed no change. Mice with transplanted Ehrlich ascites, an purified substance from a tumor (no details), histidine glutamine, and canavanine led to increased mitoses in tumor cells. Canavanine (100 µg/day) for 10 days after s.c. transplantation of Ehrlich ascites sarcoma in mice led to 10-fold enlargement of tumor compared to

controls. The authors state that the toxic substance in tumors not only initiates impairment of metabolism in cancer-bearing animals but also has an essential relationship in the proliferation of tumor cells and that guanidine derivatives could be among the biochemical constituents in tumors which have accelerating effects on tumor growth.

63-820 THE INDUCTION OF SARCOMAS IN THE COLON OF RATS BY INTRALUMINAL APPLICATION OF HYDROCARBONS. (E.) Stevenson, J. L. (Dept. Path., Ohio State U., Columbus) and E. von Haam. Cancer Res. 23(4):569-570, 1963.

When a string impregnated with 3,4-benzpyrene (BP) or 20-methylcholanthrene (20-Me) was surgically placed in the descending colon of young adult Wistar rats for 18 mo., invasive adenocarcinomas, *in situ* carcinomas, spindle cell sarcomas, and lymphosarcomas developed in 1/56, 1/56, 0/56 and 4/56, resp., of BP-treated rats and 0/56, 1/56, 2/56 and 0/56, resp., of 20-Me-treated rats. When the string was placed in the transverse colon, the values were: 0/56, 0/56, 1/56 and 3/56, resp., for BP-treated rats and 0/56, 0/56, 0/56 and 2/56, resp., for 20-Me-treated rats. After admin. of 3 ml of olive oil enemas containing 0.5% BP or 20-Me x 2/wk. for a yr., lymphosarcoma developed in 2/20, and 1/20, resp.; no tumors developed in rats similarly treated with croton oil or pure olive oil. The failure of carcinogen-impregnated string to induce tumors in the colon is thought to be due to the lack of contact of the carcinogen with the epithelium.

63-821 ACTIVE PRINCIPLES OF CROTON OIL. I. BIOLOGICAL ASSAYS FOR THE QUANTITATIVE MEASUREMENT OF THE INFLAMMATORY, COCARCINOGENIC, AND TOXIC EFFECTS. (Ger.) Hecker, E. (Max-Planck Inst. Biochem., Munich, Germany). Zschr. Krebsforsch. 65(4):325-333, 1963.

Croton oil (0.6 µg in acetone) deposited on the inner side of the ear, induced no inflammatory reaction at 24 hr. in 3 month-old, inbred, Sandoz-Basel (SaB) mice; 1.2 µg induced slight, localized erythema; 2.4 µg induced marked erythema; 4.8 or 9.6 µg induced severe erythema of the entire outer ear, frequently accompanied by secondary epidermal hyperplasia. Equivalent effects were obtained with 4 commercial brands of croton oil; similar, inflammatory reactions were not seen, however, after deposition of 154 µg sorbic alcohol, 96 µg extract of *Lithraea caustica*, or 768 µg semecarpus nut liquid. Deposition of 3.6 µg croton oil resulted in virtually total destruction of the sebaceous glands at the site of deposition, with spontaneous regeneration which began after 4 days or more. One wk. after shaving a dorsal area in SaB mice, aged 6, 10-13, or 13-16 wk., the animals received 300 µg

9,10-dimethyl-1,2-benzanthracene in 0.1 ml acetone topically to the shaved area, followed 1 wk. later, by croton oil DAB6 (0.1 ml of a 0.5% acetone soln. topically 2 x/wk. for 12 wk.). The number of wk. of total latency, wk. to tumor development in 100% of animals treated, and wk. to the beginning of the "plateau" when no further tumors were developed, was tabulated as follows: in 1 group of 6 week-old mice - 3, 9, 11; in a 2nd group - 4, 8, 11; in 10-13 week-old mice - 5, 10.5, 12; and in 13-16 week-old mice - 6, 12 (80% with tumors), not determined. The period of observation was not continued beyond 12 wk. In general, these results were reproducible, but with considerable variations of individual response in treated mice. The cocarcinogenic activity of different commercial brands of croton oil was highly variable, in terms of all parameters assayed (above); with "London" most active, "Hamburg" least active, and the other two with intermediate values. When croton oil DAB6 (in polyethylene glycol 400 and 10% alcohol) was inj. into the abdominal lymph sac of female frogs (*Rana esculenta*), the 6-12 hr. LD₅₀ was 6 mg/50 g; that of croton oil (London) was 3-4 mg/50 g; 6-12-hour deaths were due to abdominal hemorrhage, while animals surviving more than 12 hr. died later, due to the sequelae of acute inflammatory reactions.

63-822 GENOME DIVISION DURING THE DEVELOPMENT OF BUTTER YELLOW-INDUCED CANCER OF THE RAT LIVER. (Ger.) Glass, E. (Inst. Forest Bot., Albert-Ludwigs-U., Freiburg i. Br., Germany). *Zschr. Krebsforsch.* 65(4):409-424, 1963.

During the establishment of rat hepatoma by the feeding of butter yellow, the total dose received (as an index of increasing cancerization) was tabulated in relation to (1) the percentage incidence of genome divisions in metaphase, (2) the percentage of such divisions which were unusual (i.e., other than 21:21), and (3) the percentage which were highly unusual (i.e., virtually never encountered in normal rat liver). Tabulations for cells in euploid metaphase were as follows, resp.: (A) untreated controls - 29.1, 5.8, 0.0; (B) 220 mg - 44.9, 10.6, 0.0; (C) 320 mg - 52.3, 16.9, 0.8; (D) 400 mg - 56.3, 23.1, 0.6; (E) 640 mg - 65.8, 28.9, 1.5; (F) 790 mg - 72.4, 34.7, 2.2; (G) 1020 mg - 79.1, 48.6, 1.8; (H) incipient hepatoma (not macroscopically confirmable) - 48.7, 57.9, 13.2; (I) hepatoma macroscopically evident - 67.5, 69.2, 15.4; (J) hepatoma fully established - 61.4, 45.1, 11.8. Comparable tabulations for cells in aneuploid metaphase were: (A) 29.7, 4.5, 0.0; (B) 68.7, 9.1, 0.0; (C) 72.7, 13.9, 4.2; (D) 67.4, 15.5, 1.0; (E) 82.3, 18.1, 3.4; (F) 84.8, 18.5, 4.9; (G) 82.7, 29.2, 6.5; (H) 59.9, 46.5, 26.7; (I) 59.2, 52.1, 27.9; and (J) 73.0, 40.6, and 15.1, resp. For cells in diploid metaphase, tabulations were made for the same dose levels in terms of 4 possible variations in genome division (42 = 42, 42 = 21:21,

42 = 21:11:10; and aneuploid divisions such as 42 = 27:15). The resulting tabulations were as follows: (A) 85.5, 12.0, 2.2, 0.3; (B) 75.0, 18.5, 5.5, 1.0; (C) 59.0, 24.8, 5.3, 10.9; (D) 56.1, 28.7, 3.0, 12.2; (E) 47.9, 27.3, 1.4, 23.4; (F) 33.8, 35.5, 5.2, 25.5; (G) 21.6, 29.8, 2.7, 45.9; (H) 65.7, 14.3, 0.0, 20.0; (I) 51.6, 9.7, 0.0, 38.7; (J) 52.6, 31.5, 0.0, 15.9. Additional studies confirmed that both the incidence of genome division and the relative frequency of aneuploid numbers not seen in controls (e.g., 18, 48) increased with both increasing ploidy and increasing cancerization; and that this trend was sharply reversed, at all levels of ploidy, with the first establishment of the hepatoma, prior to its becoming macroscopically evident. Of special interest was the fact that 84% of all "new" aneuploid numbers contained functional groups of 6 chromosomes each, which were capable of being added to a complete genome to create a functionally competent, aneuploid nucleus.

63-823 CANCER THERAPY: A POSSIBLE NEW APPROACH (E.) Szent-Györgyi, A. (Inst. Muscle Res., Marine Biol. Lab., Woods Hole, Mass.), A. Hegyeli and J. A. McLaughlin. *Science* 140: 1391-1392, 1963.

A growth promoting substance (promine) and a growth inhibiting one (retine) have been isolated in Krebs 2 ascites tumors, thymus, aorta, muscle and tendon; both appear to be of low molecular wt., highly active and nontoxic to animals. Growth promotion and inhibition depended on a balance of the 2, e.g., for cancer regression the ratio of retine to promine had to be doubled by retine inj. Blood cell producing organs appeared to be immune to the action of the 2 substances. Retine appears to contain 1 or more unstable links. More promine and less retine were found in the aortas of old than young animals. In young animals, tendons and aortas show a large excess of retine compared to promine, possibly accounting for the low tumor incidence in these tissues. Adequate admin. of retine has resulted in experimental tumor regression. Methods for the isolation of the 2 substances are presented.

63-824 GROWTH AND CELLULAR CONSTITUENTS. (E.) Szent-Györgyi, A. (Inst. Muscle Res., Marine Biol. Lab., Woods Hole, Mass.), A. Hegyeli and J. A. McLaughlin. *Proc. Nat. Acad. Sci. U.S.A.* 49(6):878-879, 1963.

See CRA 1(5):#823, 1963.

63-825 A PATTERN OF CHANGE IN TUMOR-CELL POPULATIONS *IN VIVO*. (E.) Roberts, D. C. (Div. Exp. Biol., Imperial Cancer Res. Fund, Mill Hill, London). *Brit. J. Cancer* 17(1):142-148, 1963.

Analysis of the daily fluid samples from a serially transplanted strain-specific ascites subline

a naturally occurring epithelioma (255/B1 from C/57 black mouse) revealed that the proportion binucleate cells increased throughout the life of each generation and that the increase was not cumulative from one generation to the next. Clear changes were measured by the method of weighing the paper outlines of projected images. The first and last samples of 3 generations showed no major difference in population. In the 1st sample of the 1st generation, the mode was 3 x the volume of a postmitotic nucleus of a normal cell (V); in the 2nd sample, the mode was in the 2-4 V range; in the last sample a similar distribution to the 1st was found but with consistently smaller nuclear sizes. In the 2nd generation, the 1st sample had a mode of 4-8 V; the 3rd, a mode of 2-4 V; the 2nd sample was intermediate; and the final sample approximated the 1st. Similar measurements were made for a benzpyrene-induced sarcoma C/56AA.

826 A FURTHER STUDY OF BLADDER IMPLANTATION IN THE MOUSE AS A MEANS OF DETECTING CARCINOGENIC ACTIVITY: USE OF CRUSHED PARAFFIN WAX OR STEARIC ACID AS THE VEHICLE. (E.) Bonser, G. M. (Dept. Exp. Path., U. Leeds, England), E. Boyland, E. R. Busby, B. Clayton, P. L. Grover and J. W. Jull. Brit. J. Cancer 17(1):127-136, 1963.

The incidence of carcinoma was determined after implantation of agent-impregnated paraffin pellets into the bladders of mice. In 2 experiments, 20-methylcholanthrene, which was very strongly carcinogenic, produced tumors in 18/37 (48%) and in 22/38 (58%). Carcinogenic action was inhibited by 2-naphthylhydroxylamine, which induced carcinomas in 13/62 (21%), bis(2-amino-naphthyl)sodium phosphate 15/47 (32%), 2-amino-1-naphthol HCl 5/30 (16.7%), 1-phenylazo-naphthol 7/42 (17%) and Ponceau 3R 5/33 (15%). The following were inactive (did not produce significantly more tumors than controls): (2-amino-1-naphthyl)sodium phosphate (in stearic acid), 4'-hydroxy-4-aminodiphenyl HCl, 2-amino-1-fluorenone HCl, 3-amino-2-fluorenone HCl, 2-amino-3-fluorenone HCl, 7-amino-2-fluorenone HCl, 4-methoxy-4-aminodiphenyl HCl, 1-naphthylamine HCl, 3-hydroxybenzidine HCl, Ponceau 2R and 1-amino-2-naphthol-1:2-naphthaquinone. Compounds which gave intermediate yields of tumors and should be tested were: 3-hydroxy-4'-methoxy-4-aminodiphenyl HCl, 4:4'-diamino-3-diphenyl hydrogen phosphate (benzidine-3-sulfuric acid) and 4-nitrostilbene. The validity of the technic of bladder implantation is considered to be fully established.

827 EVALUATION OF THE CARCINOGENICITY OF AMINOFLUORENOLS BY BLADDER IMPLANTATION. (E., Abstract) Larson, D. M. (Dept. Biol. Chem., U. Minnesota, Minneapolis), J. Gutmann and C. C. Irving. Proc. Am. Cancer Res. 4(1):37, 1963.

The bladders of Swiss female mice were implanted with paraffin pellets which contained the hydrochlorides of 2-amino-1-fluorenone, 2-amino-3-fluorenone, 2-amino-5-fluorenone, 2-amino-7-fluorenone, 2-fluorenamine, or 1-amino-2-naphthol. After 40 wk. no bladder carcinomas had developed and the mucosal epithelium of both experimental and control (paraffin alone) animals showed similar inflammatory and hyperplastic changes. Radioactivity measurements after implantation with 2-amino-1-fluorenone-1-¹⁴C indicated that about 30% of the compound disappeared from the pellets in 25 wk., while the remainder was unchanged. In contrast, implantation with 1-amino-2-naphthol-H³ resulted in rapid decomposition to unknown compounds.

63-828 CARCINOGENICITY OF 2-NAPHTHYLHYDROXYLAMINE. (E.) Boyland, E. (Chester Beatty Res. Inst., Royal Cancer Hosp., London), C. E. Dukes and P. L. Grover. Brit. J. Cancer 17(1):79-84, 1963.

2-Naphthylhydroxylamine (50 mg/kg in arachis oil; 2 x/wk. for 3 mo. i.p.) in 15 Chester Beatty random inbred strain albino rats induced 6 abdominal sarcomas, 3 abdominal carcinosarcomas of diverse histological types and 1 lymphosarcoma. An identical dose of 2-naphthylamine induced sarcomas in 2/14 and possibly a salivary gland tumor in 1/14. The results agree with the hypothesis that 2-naphthylamine and some other aromatic amines exert their carcinogenic action after metabolic conversion to hydroxylamine derivatives.

63-829 RHABDOMYOSARCOMAS INDUCED BY NICKEL SULPHIDE IN THE RAT. (E., Abstract) Noble, R. L. (Cancer Res. Ctr., U. British Columbia, Vancouver, Canada) and V. Capstick. Proc. Am. Assn. Cancer Res. 4(1):48, 1963.

Nickel sulfide, inj. i.m. by the technic of J. R. W. Gilman, induced rhabdomyosarcomas rapidly and in a high percentage of rats from various (unspecified) strains. The transplanted tumors grew rapidly and served as models for testing various chemotherapeutic agents such as vinca alkaloids and anabolic and catabolic hormones. Cortisol was found to be an effective inhibitor of tumor growth.

63-830 STUDIES OF NICKEL CARCINOGENESIS: ALTERATIONS OF RIBONUCLEIC ACID FOLLOWING INHALATION OF NICKEL CARBONYL. (E.) Sunderman, F. W., Jr. (Dept. Med., Jefferson Med. Coll., Philadelphia, Pa.). Am. J. Clin. Path. 39(6):549-561, 1963.

In Wistar rats sacrificed 24 hr. after nickel carbonyl (0.6 mg/l of air inhalation for 30 min.), the conc. of nickel in the NaCl precipitable (PF) fraction of lung RNA increased from 110 (controls) to 270 µg/g RNA, whereas the conc. of nickel in the NaCl soluble (SF) of lung RNA

decreased from 340 (controls) to 230 $\mu\text{g/g}$ RNA. The conc. of nickel in the PF of liver RNA increased from 59 (controls) to 160 $\mu\text{g/g}$; that in the SF was not significantly altered: 120 (controls) to 110 $\mu\text{g/g}$. Following nickel exposure, the PF of lung and liver RNA underwent a significant decrease in the maximal absorbance ratio (A_{max}) with relatively no change in the temperature of the midpoint of phase transition (T_m), whereas the SF of lung RNA underwent a significant decrease in T_m with relatively little change in A_{max} . The SF of liver RNA demonstrated little change in T_m and A_{max} . Diminution of A_{max} was consistent with increased metal bonding in RNA, whereas diminution in T_m was consistent with disruption of hydrogen bonds. Such alterations may point to a mechanism of pulmonary carcinogenesis.

- 63-831 EXPERIMENTAL STUDY ON CARCINOGENICITY OF HYDROCARBONS IN PULMONARY CARCINOMA. (Jap., Abstract) Oshima, T. (Tokyo Sch. Med. Dent.), K. Takemoto and K. Namie. Nippon Eiseigaku Zasshi (Jap. J. Hyg.) 18(1):142, 1963.

3,4-Benzpyrene (BP), combined with coal dust, was inj. intratracheally in rats. The frequency of induced tumors was less than that induced by 20-methylcholanthrene. When BP (3 mg/day) was given to female rats weighing 100 g, no tumors were found during 18 mo. of observation. BP (5 mg/day) for over 9 mo. led to some evidence of carcinogenesis; all tumors were epidermoid in origin, none arose from mesenchymal tissue.

- 63-832 COMPARATIVE EFFECTS ON RAT LIVER CELLS AFTER DIMETHYLNITROSAMINE, 2-FLUORENAMINE, OR PREDNISOLONE TREATMENT STUDIED BY ELECTRON MICROSCOPY. (E.) Gustafsson, R. G. (Wenner-Gren Inst., Stockholm) and B. A. Afzelius. J. Nat. Cancer Inst. 30(5):1045-1075, 1963.

Electron microscopic studies of liver cells from male Wistar rats treated for 20 hr., p.o. or i.p. with dimethylnitrosamine (D; 20 mg/kg), 2-fluorenamine (F; 450 mg/kg), or prednisolone (P; 50 mg/kg) revealed a disorganization of the cisternal endoplasmic reticulum (e.r.) and a decrease in the number of membrane-bound particles after D, or F; an increase in the number of free ribosomes after F or P; enlargement of the spongy e.r. by all 3 compounds accompanied by an increase in the morphological glycogen; a transitional form between agranular spongy e.r. and granular cisternal e.r. after P admin. Findings were compared to those of controls which had been starved for the duration of the experiment. The hypertrophy of the spongy e.r. may be associated with gluconeogenesis. The author suggests that D and F increase the number of free ribosomes, amount of spongy e.r., and glycogen by potentiating the action of glucocorticoids on the liver cells.

- 63-833 A VIRUS RESEMBLING THAT OF ENDEMIC PNEUMONIA ISOLATED FROM LYMPHOSARCOMA INDUCED IN SWISS MICE BY 9,10-DIMETHYL-1,2-BENZANTHRACENE. (E.) Bather, R. (Nat. Cancer Inst., U. Saskatchewan, Saskatoon, Canada) and J. Cushing. Acta Un. Int. Cancr. 19(1-2): 411-414, 1963.

A cytopathogenic virus characterized as that of mouse endemic pneumonia was found in lymphosarcomas induced in newborn Swiss mice by 9,10-dimethyl-1,2-benzanthracene (DMBA). The virus has been passaged through mouse embryo cultures for more than 20 generations without loss of cytopathogenic effect (CPE); extracts from a transplanted tumor also remained active. Similar CPE was produced by extracts of normal adult lung but not by spleen, liver, kidney or thymus; any CPE produced was eliminated after change of medium. In 146 newborn mice inoc. with medium from tumor-treated cultures (1 ml s.c.), 35.6% died of endemic pneumonia ($P < .01$); in 144 given medium from spleen-treated cultures, 14.6% died. It is suggested that the spleen extract group may have been cross-contaminated. Inoc. of virus into newborn hamsters produced a similar respiratory disease but has had no influence on the induction of tumors with DMBA for over 2 yr. Of 116 mice receiving the tumor extract, 22.4% developed mammary tumors compared to 13.5% in 133 receiving spleen extract ($P = 0.05$). The total of tumors found in both groups was 28.5% and 15.1%, resp., ($P = 0.01$). No evidence of enhancement of DMBA tumor formation by virus has been found.

- 63-834 ELECTRON MICROSCOPY OF METHYLCHOLANTHRENE-INDUCED (MC) HEPATOMA AND AN ASSOCIATED LEUKEMIA. (E., Abstract) Dmochowski, L. (U. Texas M.D. Anderson Hosp., Houston, Texas) F. Padgett, J. A. Sykes, R. Liebelt and A. Lieber. Proc. Am. Assn. Cancer Res. 4(1):16, 1963.

Electron microscopic examination of spontaneous or of methylcholanthrene-induced (20-Me) hepatomas in CBA mice failed to reveal any virus particles. In transplanted 20-Me hepatomas occasional doughnut particles of 100 m μ diameter were observed. Passage of these transplanted tumors in tissue culture resulted in the appearance of numerous doughnut-type particles and fully formed virus particles (120 m μ with a nucleoid of 70 m μ). Electron microscopy of leukemic spleens from animals in which the hepatomas had regressed or had been excised, and of the same spleens after passage in tissue culture gave the same findings. Numerous virus particles were also observed in spleens of mice with leukemias induced by passage of cells from leukemic spleens of mice in which hepatomas had regressed.

- 63-835 MOLECULAR SIZE PROFILES OF THE SOLUBLE PROTEINS OF NORMAL AND PRENEOPLASTIC LIVERS OF RATS. (E., Abstract) Young, E. M.

Inst. Cancer Res., Philadelphia, Pa.), R. A. S. Sorof. Proc. Am. Assn. Cancer Res. 4(1):74, 1963.

The principal azo and fluorenyl conjugates of the soluble liver proteins of male rats fed 3'-methyl-4-dimethylaminoazobenzene for 2½ wk. or 2-acetyl-1-fluorene for 5 wk. followed by acetylaminofluorene-9-C¹⁴ 48 hr. before sacrifice belong to most identical electrical charge classes. The conjugates have now been shown to belong to the same molecular size group as well.

836 EXPERIMENTAL CARCINOGENESIS IN THE KIDNEY OF RANA PIPIENS. (E., Abstract) Strauss, E. (Graduate Sch. Arts and Science, New York U., New York) and G. M. Mateyko. Proc. Am. Assn. Cancer Res. 4(1):66, 1963.

Single subcapsular inj. of creosote oil, 5,7-methyl-1,2-benzacridine, 3,4-benzpyrene or 1-methylcholanthrene (0.3-0.5 mg in olive oil) had toxic effects in leopard frogs grossly free of renal carcinomas at the time of inj. Inj. of 2,5,6-dibenzanthracene (same doses) caused, within 3 mo., white nodules in the kidney, liver and lung, but these had no similarity to the spontaneous Lucké adenocarcinoma. After 6 mo., however, typical Lucké tumors developed. p-Dimethylaminoazobenzene (same doses as above) caused renal neoplasms histologically similar to Lucké's adenocarcinomas at 3-9 wk. The tumors contained multiple, basophilic, gland-like papillary projections without encapsulation. Alkaline phosphatase activity was absent in neoplastic cells and reduced in the surrounding intact renal cells.

837 THE IN VIVO LABELING OF LIVER RIBONUCLEIC ACID BY p-DIMETHYLAMINOAZOBENZENE-1'-C¹⁴ (DAB). (E., Abstract) Broquing, F. (Dept. Path., U. Pittsburgh Sch. Med., Pittsburgh, Pa.) and E. Farber. Proc. Am. Assn. Cancer Res. 4(1):41, 1963.

Admin. of p-dimethylaminoazobenzene-1'-C¹⁴ (DAB; 1.28 mg = 5.7 µmoles, 10 µC) to male white star rats by gastric intubation yielded radioactivity equivalent to 11 µmoles/mg and 19 µmoles/mg purified liver RNA and liver protein, resp. The radioactivity in RNA or protein was not removed by refluxing with boiling ethanol-ether for 22 hr., or by trypsin treatment. About 50% of the radioactivity in the RNA became dialyzable after RNase treatment. The incorporation of a comparable dose of aniline-1-C¹⁴ into liver RNA and protein was less than 1/25 and 1/6, resp. Equal doses of the labeled DAB admin. to the control rat, which is resistant to DAB-induced liver cancer, resulted in the binding of 11.4 µmoles/mg of liver protein and 3.0 of RNA. These results are in agreement with the conclusion that liver carcinogenesis DAB may bind to RNA as well as to protein.

63-838 CYTOLOGICAL AND CYTOCHEMICAL ALTERATIONS IN THE RESPIRATORY TRACT OF MICE AFTER EXPOSURE TO CIGARETTE SMOKE, INFLUENZA VIRUS AND BOTH. (E.) Leuchtenberger, C. (Inst. Gen. Bot., Swiss Fed. Inst. Technol., Zurich), R. Leuchtenberger, F. Ruch, K. Tanaka and T. Tanaka. Cancer Res. 23(4):555-565, 1963.

Histological, cytological and cytochemical studies of sequential changes in the respiratory tract of CF mice after exposure to inhalation of cigarette smoke (CS; ½-3 cigarettes/day x 30-420) disclosed marked atypical proliferative lesions in the small bronchi in 24% of females (F) and 12% of males (M). Mice receiving a mild infection with PR8 influenza virus (IV) had these lesions in 32% F and 24% M, compared to mice receiving both treatments, 68% F and 70% M. Mild lesions developed in 8% of F and 6% of M controls. Frequency of bronchitis of a marked necrotizing type with visible viral reactivity for controls and CS was 0%; for IV mice, 37% F and 14% M; for mice receiving both treatments, 34% F and 38% M. Atypical proliferative lesions manifested themselves mainly in the small bronchi and bronchioles and were accompanied by intracellular DNA, RNA, and protein increase. In IV mice or in IV + CS mice, an increase in nuclear and cytoplasmic RNA agglomerations, associated with absence of mitosis and cell destruction prior to atypical proliferation was noted. CS + IV males showed a high percentage of marked metaplasia (29%) and marked transgression of epithelial cells into lung parenchyma (33%) compared to similarly treated females (9 and 18%, resp.).

63-839 OBSERVATIONS ON SKIN CANCER AMONG REFINERY WORKERS. LIMITED TO MEN EXPOSED TO HIGH-BOILING FRACTIONS. (E.) Wade, L. (Sloan-Kettering Inst. Cancer Res., New York). Arch. Environ. Health (Chicago) 6(6):730-735, 1963.

Among 1077 matched pairs of workers in 3 refineries (in La., N.J. and Md.) during the period 1949-61, 46 neoplasms occurred in the group exposed to high boiling aromatic petroleum fractions compared to 45 in the nonexposed group. Skin lesions constituted 58.7% (27/46) of neoplasms in the exposed group and 53.5% (24/45) of the controls. The distribution of skin cancers of the basal cell type in the exposed group was 15 on face-head-neck, and 2 on the extremities; in controls 1 was on the lip; 15 on face-head-neck and 0 on extremities. The distribution of squamous cell carcinomas was, in exposed workers, 6 on lip, 4 on extremities; in controls, 3 on lip, 4 on face-head-neck, and 1 on the trunk. All lesions of the extremities occurred in the exposed group yet no relationship to job was apparent when case histories were studied. The same number of lesions appeared in each of the 2 groups before age 45 and after age 50. The author offers 2 explanations for the findings: (1) the high-boiling aromatic fraction was not

carcinogenic to man; (2) the extent or frequency and duration of exposure was inadequate to produce lesions. Prolonged observation of the exposed group is necessary to establish a more definitive answer.

- 63-840 SUCCINIC DEHYDROGENASE LEVELS IN LIVERS OF RATS DURING EARLY FEEDING OF 4-DIMETHYLAMINOAZOBENZENE; A REINTERPRETATION OF THE BIOCHEMICAL DATA. (E.) Jones, G. R. N. (Dept. Path., Roy. Coll. Surg. England, London). *Brit. J. Cancer* 17(1):153-161, 1963.

Levels of succinic dehydrogenase (SDH) estimated by the anaerobic methylene blue (MB) technic in left lobes of livers of male August strain rats fed 4-dimethylaminoazobenzene (DAB; 0.06% in a 20 g low-protein diet daily) fell from a QMB of 24 (μ l hydrogen equivalent to MB reduction/mg dry wt./hr.) at 31 days after DAB feeding to 11 and 10, after 95 and 151 days, resp., compared with controls for the same time intervals of 20, 22, and 22, resp. Similar changes were observed in the right posterior and anterior, ventral, and caudal lobes. The decreased SDH activity was correlated with dilution of SDH-rich parenchymal cells by proliferation of bile duct and connective tissue cells which appear to have low or negligible SDH activity.

- 63-841 CARCINOGENICITY AND METABOLISM OF 2-NAPHTHYLAMINE. (E., Abstract) Conzelman, G. M., Jr. (Christ Hosp. Inst. Med. Res., Cincinnati, Ohio), K. Springer, L. E. Flanders, III and D. W. Crout. *Proc. Am. Assn. Cancer Res.* 4(1):12, 1963.

2-Naphthylamine was admin. in daily oral doses of 6.25-25.0 mg/kg for 6-18 mo. to 17 dogs and 18 monkeys. In dogs bladder lesions ranging from minute papillomas to multiple invasive carcinomas developed in animals which received 25 mg/day or greater for 12 mo. or longer. The bladders of rhesus monkeys on similar dosages were normal. Examination of iced urine collected at frequent intervals revealed that dogs excrete about 70% of the ingested amine as the ortho-hydroxy derivative, while monkeys only excrete 19% in that form. In monkeys the major metabolite was 2-acetamido-6-naphthyl glucuronic acid, which suggests that acetylation may prevent oxidation of the alpha carbon and hence compete with orthohydroxylation.

- 63-842 ENZYME LEVELS IN LIVER CELLS OF RATS FED 4-DIMETHYLAMINOAZOBENZENE (DAB) AND IN PRIMARY LIVER TUMORS. (E., Abstract) Lamirande, G. De (Montreal Cancer Inst., Canada). *Proc. Am. Assn. Cancer Res.* 4(1):15, 1963.

The activities of 5'-nucleotidase, inosine phosphorylase and uricase in the parenchymal cells of rat livers were decreased 80%, 50% and 50%,

resp., after 12-16 wk. of feeding with 4-dimethylaminoazobenzene. Decreases of 60%, 25% and 30% were observed in nonparenchymal cells. Guanase activity was not affected. In primary liver tumors more pronounced decreases were observed in both cell types.

- 63-843 CELLULAR POPULATIONS AND MITOTIC ACTIVITY IN PRENEOPLASTIC LIVER PARENCHYMA (E., Abstract) Daoust, R. (Montreal Cancer Inst. Canada) and F. Molnar. *Proc. Am. Assn. Cancer Res.* 1(4):13, 1963.

Rats fed 4-dimethylaminoazobenzene were examined for histological liver changes in sections stained with toluidine blue. At early stages of feeding hypobasophilic cells were seen in central vein areas. These did not divide, became necrotic and eventually disappeared. At all stages of feeding basophilic cells were observed in portal areas. In treated rats these cells had an incidence of mitosis of 0.23%, as compared with 0.0% in normal liver. At later stages of feeding hyperbasophilic cells were observed, apparently derived from the previous population. These cells exhibited many features of cancer cells including a mitotic activity of 0.81% which was intermediate between that of the surrounding parenchyma (0.2%) and that of the hepatomas (1.86%).

- 63-844 CARCINOGENESIS IN MARSH MICE BY TESTICULAR INJECTION OF CHOLESTEROL ALPHAXIDE. (E., Abstract) Bryson, G. (Cottage Hosp., Santa Barbara, Cal.) and F. Bischoff. *Proc. Am. Assn. Cancer Res.* 4(1):8, 1963.

Testicular inj. of cholesterol alpha oxide (CAO; 10 mg/mouse in saline) into Marsh mice produced scrotal fibro- or myosarcomas in 7/89. No tumors developed in 81 controls receiving saline, or in 34 controls receiving sesamol (0.4 mg), also by testicular inj. Mice receiving CAO + sesamol and CAO alone developed sarcomas in 1/33 and 2/33, resp. The CAO caused fibrosis of the tunica albuginea in 2 mice, a spermatogenic arrest in 1, and fibrosis in dosed areas in 3. Sesamol produced focal areas of calcification and fibrosis in 35% of the dosed animals, and also aspermatogenesis. CAO was detected in 54% of the dosed areas at 18 mo. of age, when the experiment was terminated. Two undifferentiated carcinomas were found in the mesenteric lymph nodes in the CAO treated series, suggesting possible activity at a distal site.

- 63-845 EXPERIMENTAL STUDY OF THE DEVELOPMENT OF CANCEROUS EPITHELIUM WITHIN THE RECTAL WALL. (Rus.) Lavrenko, V. V. (S. M. K. Army Med. Acad. (Order Lenin), Leningrad). *Arkh. Anat.* 44(5):84-95, 1963.

After topical admin. of 3,4-benzpyrene (0.5-1.0% soln. in benzene or oil, 3 x/wk.) to the rectum of 119 white mice, observations were made at

ious intervals up to 13 mo. Gross examination after the 1st application revealed perianal hair loss, hemorrhages and thickening and cracking of the skin, followed after some days by the appearance of warts. After 180-200 days, 52.7% of the survivors had developed planocellular carcinoma or sarcoma of the rectoanal or perianal region. Among the tumors were 27 cancers which showed various degrees of differentiation; DNA and RNA content was increased. Nuclear size was compared utilizing the technic of weighing the nuclei of the projected outlines, ranking each group from the largest to the smallest and reporting nuclei numbers 1, 6, and 10. In controls these values were 0.070, 0.048 and 0.040 g; the nuclei from treated cells after 13 mo. had values 0.240, 0.090, and 0.050 g. Sarcomas developed 2/119 after 6 and 9 mo. After a single application, histological examination revealed changes in the rectal wall within periods of 10 min. to 24 hr.

846 CARCINOGENIC EFFECT OF HUMAN SARCOMA EXTRACTS ON RATS. (Rus.) Ageenko, V. I. (P. A. Herzen State Res. Inst. Oncol., Moscow). Vop. Onkol. 9(6):42-51, 1963.

Eight Wistar rats, age 1-6 days, received a 1-ml free extract of human sarcoma (0.5-1.0 ml daily, with repetition of the dose after 21 days). 16/145 which developed tumors and in 6/145 which developed leukemias, first cancers were detected after 10.4-17.6 mo. after admin.; average latent periods ranged from 15.9-18.2 mo. First pregnancies appeared after 7.2-14.5 mo. in irradiated rats (18/121 tumors, 10/121 leukemias). In rats given either 20-methylcholanthrene or 9,10-dimethyl-1,2-benzanthracene, each 0.005 g s.c. (30/149 tumors and 12/149 leukemias). Average latent periods ranged from 14.3-15.6 mo. Irradiation of the extract with 125,400 r or heating to 90°C for 40 min. resulted in inactivation as did treatment with rabbit antiserum against human sarcoma. UV did not significantly alter carcinogenicity; ether led to partial inactivation. Cerebral passages (6) in rats, or treatment with glycerol or enzymes (RNase, trypsin, papain, lipase) did not inhibit carcinogenicity. Extracts (both heated and unheated) from various benign and malignant human tumors (tested in 307 and 667 rats, resp.) were inactive except one of a solid ovarian cancer that induced tumors in 2/15.

847 OCCUPATIONAL BRONCHOGENIC PULMONARY CANCER IN WORKERS EXTRACTING, ISOLATING AND REPROCESSING NICKEL ORE. (Rus.) Menskii, S. V. Vop. Onkol. 9(6):130-131, 1963.

In contrast to the reports of English authors, reports on the incidence of respiratory tract cancer in nickel workers are available in the USSR. In the author's own material, bronchogenic carcinoma does appear in these workers due

to deposits of nickel compounds upon the pulmonary tissues. Malignant growth starts after chronic inflammation of the bronchial tree. Less frequent is skin cancer, and no report of cancer of the trachea is found in Noril'sk (USSR) workers. The author states that since nickel is known to produce experimental cancer and eczema, it should be reported as a carcinogen. The prevention of cancer in these workers is possible, particularly when detected in the early stages.

63-848 SPONTANEOUS REGRESSION OF INDUCED MAMMARY TUMOURS IN RATS. (E.) Young, S. (Div. Path., Imper. Cancer Res. Fund, London). Brit. J. Cancer 17(1):85-89, 1963.

After admin. of 9,10-dimethyl-1,2-benzanthracene (DMBA; 50 mg in 2 ml corn oil p.o.) to female Sprague-Dawley rats 50 ± 1 days of age, palpable tumors developed in 86/139 within 31-100 days. Tumors were of 3 types: growing (G), 20.4%; static (S), 52.5%; and spontaneously regressing (SR), 27.1%. S and SR tumors appeared first and had a significantly slower rate of growth than G tumors ($p < 0.05$). In tests of hormones, the agent was given s.c. daily, 6 days/wk. x 3-4. Estradiol benzoate (E; 2 µg) and progesterone (P; 8 mg) admin. to 29 rats bearing S or SR tumors stimulated 3/29 to further growth. The same dose of E and P after oophorectomy stimulated 1/25 to growth compared with 9/13 post-oophorectomy regressions which were reactivated by the same dose. E, P, bovine growth hormone (0.5 mg) and cortisone (10 mg) given together failed to reactivate SR tumors. (See also CRA 1(5):#849, 1963.)

63-849 THE HISTOLOGY OF INDUCED MAMMARY TUMOURS IN RATS. (E.) Young, S. (Imperial Cancer Res. Fund, London), D. M. Cowan and L. E. Sutherland. J. Path. Bact. 85(2):331-340, 1963.

Earlier results are presented of the work reported in CRA 1(5):#848, 1963. After p.o. admin. to female rats of 9,10-dimethyl-1,2-benzanthracene (DMBA) in doses of 20, 25, 32 and 40 mg, all survived 1 yr.; mammary tumor incidence was 1/4, 4/5, 5/5 and 5/5, resp. In another experiment after 60, 80, and 100 mg, 1 yr. survivors numbered 5/6, 2/6, and 3/6, resp.; tumor incidence was 3/5, 2/2, and 2/3, resp. Tumor regression in treated rats occurred in 43/53 following oophorectomy; histological changes characteristic of regression were observed within 1-2 wk. in 18/22. Actively growing areas of regressing tumors were believed to be hormone insensitive. 17-β-Estradiol (E; 2 µg/day s.c.) reactivated 9/19 regressing tumors. Progesterone (P; 8 mg/day) failed to reactivate 16/16 tumors. P and E admin. concurrently during oophorectomy-induced tumor regression caused further growth in 12/13 and in 6 previously insensitive to P or E alone. Compared to regressions after oophorectomy, spontaneously regressing tumors differed

both in histology and in response to P and E: only 2/26 of the latter tumors regressed after admin. of P and E, even with bovine growth hormone.

63-850 BIOCHEMICAL AND MORPHOLOGICAL CHANGES IN RAT LIVER DURING CARCINOGENESIS INDUCED BY p-DIMETHYLAMINOAZOBENZENE AND DURING ADMINISTRATION OF AMARANTH. (Rus.) Rubenchik, B. L. (Ukrainian Inst. Nutr., Kiev) and A. I. Bykorez. *Vop. Onkol.* 9(4):68-75, 1963.

Admin. of p-dimethylaminoazobenzene (DAB; 0.06% in the diet for up to 18 wk.) to adult rats produced a marked initial decrease in hepatic riboflavin, succinic dehydrogenase (SDH), lactic dehydrogenase (LDH) and catalase, while cathepsin activity increased. This general decrease in the level of oxidation was accompanied by disruption of the distribution of the liver cells, with consequent partial or complete functional disorganization, peripheral necrobiosis of the parenchymal cells, nuclear pyknosis and pronounced parenchymal fatty dystrophy. After 6-8 wk., there was some rise in SDH, LDH and catalase activity, while the riboflavin decreased to a minimum. A cathepsin with a pH optimum at 3.5 decreased while another with an optimum at pH 5.0 increased. Meanwhile, the general structure of the liver was disrupted and the lobes were no longer distinguishable. After 12-14 wk., cirrhosis developed, and after 18-22 wk., in addition to dystrophic, regenerative and cirrhotic changes, there were multiple accumulations of poorly differentiated small cells and groups of gland-like structures resembling adenomas which gradually became malignant; at this time, catalase and SDH remained below normal, while the riboflavin became normal and the cathepsin with an optimum at pH 3.5 reached a minimum. At 24-28 wk. (6-10 wk. after the end of DAB admin. and the appearance of the first liver tumors), hepatocellular and cholangiocellular carcinomas could be distinguished morphologically, although there were no biochemical differences. In these animals, there was a general parallel between the morphological changes and the alterations in SDH, catalase and cathepsin activity, but not between the morphological changes and LDH or riboflavin. Admin. of the edible dye amaranth (0.2% in the diet for up to 80 wk.) to other groups of rats produced no significant changes in either liver morphology or the biochemical variables.

63-851 CHRONIC INFLAMMATION AND THE PROCESS OF CARCINOGENESIS. (Rus.) Podil'chak, M. D. (Lvov State Med. Inst., Uk.SSR). *Vrach. Delo* (6):58-62, 1963.

Application to the clipped dorsal skin of 20 albino mice of croton oil (CRO; 1.5% in acetone 2 x/wk. x 45) resulted in the development of 5 papillomas, 2/5 (which appeared after mo.

9-12) regressed spontaneously; none developed into cancer. If the application of CRO was begun 10 days after the same area of the skin was cauterized with heat, papillomas developed in 8/20 beginning after 3-12 mo. of treatment; 1 of the papillomas developed into squamous cell carcinoma during mo. 13. Two applications of 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.5% in acetone) in 4 days produced no papillomas; however, when this treatment was followed by application of CRO for 45 wk., 12/20 mice developed papillomas, appearing in mo. 3-7, although none developed cancer. DMBA was continued 2 x/wk. for 4 mo., 4/20 mice developed carcinoma and 5/20 developed papillomas; however, the first carcinoma did not develop until 4-5 mo. after the beginning of treatment, compared to 3 mo. if the DMBA was preceded by treatment with CRO (0.5% in acetone 2 x/wk. for 2 mo.). In the last case, the CRO produced a chronic inflammatory proliferation, after which DMBA was able to produce carcinoma in 9/20 mice and papillomas in 3/20; the tumors also were larger than in mice not pretreated with CRO. Thus, in contrast to the commonly held view that the first phase in carcinogenesis is a specific, irreversible, preneoplastic change which can be produced only by a definite carcinogen, a chronic inflammatory condition (as opposed to an acute inflammation) can apparently produce preneoplastic changes which create a more favorable soil for the subsequent action of a carcinogen.

63-852 SIGNIFICANT CELLULAR PATTERNS DURING "TRANSFORMATION" OF TISSUE CULTURE CELL LINES AND DURING DEVELOPMENT OF INDUCED NEOPLASTIC PROCESS IN ANIMAL HOST. (E., Abstract) Koprowska, I. (Hahnemann Med. Coll., Philadelphia, Pa.) and M. A. R. Fernandes. *Proc. Am. Assn. Cancer Res.* 4(1):34, 1963.

Parallel studies *in vivo* and in tissue culture morphologic changes observed in exfoliated cells from the uteri of mice treated with benzpyrene revealed a sequential course of transformation (during development of epithelial dysplasia) which consisted of alterations into undifferentiated, differentiated and giant cellular elements. Cells obtained from dysplastic lesions were transformed, in tissue culture, to a stable cell line morphologically similar to another cell line developed from a transplantable squamous cell carcinoma. However, isografts of these transformed cells originating from cervical dysplasia failed to cause tumor growth.

63-853 STUDIES ON CO-CARCINOGENS AND CANCER PROMOTING AGENTS IN RATS. (E., Abstract) Shay, H. (Fels Res. Inst., Temple Univ. Sch. Med., Philadelphia, Pa.), M. Gruenstein, W. B. Kessler and L. L. Ashburn. *Proc. Am. Assn. Cancer Res.* 4(1):61, 1963.

In female Wistar rats the feeding of a synthetic diet containing 50% or 22% casein, or 50% lactalbumin, increased the incidence of mammary cancer

to 20-methylcholanthrene (20-Me; 5 mg/day, intragastrically) to 45, 47.3 and 26.3%, resp., whereas the frequency of breast cancers in 20-Me in controls fed a Rockland diet ranged from 8.7%-17.3%. The frequency of mammary cancers in animals treated with 20-Me and fed a synthetic diet + 50% egg albumin or casein was 0% and 5.0%, resp., which was identical to that of casein-fed controls not treated with 20-Me (2%).

854 INTRATRACHEAL INJECTION OF PARTICULATE CARCINOGENS INTO HAMSTER LUNGS. (Abstract) Saffiotti, U. (Div. Oncol., Chicago Med. Sch., Ill.), F. Cefis, L. H. Kolb and M. I. Grote. Proc. Am. Assn. Cancer Res. 14:59, 1963.

Intratracheal admin. to hamsters of dusts containing 3,4-benzpyrene (BP) or 9,10-dimethyl-1,2-benzanthracene (DMBA) ground with iron oxide (particle size less than 1 μ) showed that single doses of BP were eliminated completely from the lung within 1 wk. Iron oxide alone was eliminated from the lung slowly by phagocytosis; addition of BP to the iron oxide induced minimal changes in the early reaction pattern but with large doses, but addition of DMBA induced rapidly severe toxic changes. The 2 carcinogens were adherent to the iron oxide. Proliferative changes of the bronchial mucosa were also demonstrable with single or repeated doses. Cobalt oxide powders also induced hyperplasia of the bronchial epithelium when administered intratracheally.

855 THE TUMOR-ENHANCING PRINCIPLE FROM CROTON OIL AND CROTON RESIN. (E., Abstract) Van Duuren, B. L. (Inst. Industrial Hygiene, New York U. Med. Cent., New York), L. J. Aronson and E. Arroyo. Proc. Am. Assn. Cancer Res. 14:69, 1963.

Analysis of seeds of Croton tiglium for the tumor-enhancing principle of croton oil revealed that a methanol extractable croton oil fraction isolated by solvent partition promoted 88% tumors in mouse skins painted with 9,10-dimethyl-1,2-benzanthracene (DMBA) compared to 33% tumors in animals painted with the whole croton extract (DMBA). Infrared spectra of the resin showed aromatic, aliphatic C-H and ester carbonyl. Alkali hydrolysis gave 70% unsubstituted fatty acids which varied in length from C12 to C18 (straight and branched chain, saturated and unsaturated). Sixteen of the acids were identified.

856 LIVER TUMORS PRODUCED IN RATS BY FEEDING SAFROLE. (E.) Long, E. L. (Div. Pharmacol., Food and Drug Admin., Washington, D.C.), A. A. Nelson, O. G. Fitzhugh and W. H. Hansen. Arch. Path. (Chicago) 75(6):604, 1963.

Osborne-Mendel rats (evenly divided as to sex) were fed varying amounts of 4-allyl-1,2-methylenedioxybenzene (safrole; 100-5000 ppm in Purina diet for 2 yr.). Primary hepatic tumors appeared in 19/50 (7 males) fed 5000, in 8/50 (2 females) fed 1000, in 3/50 (2 males) fed 500, in 1/50 (male) fed 100, and also in 3/50 (3 males) controls. Multiple tumors were most frequent (12) in animals fed 5000 ppm safrole, there were 2 instances in the group which received 1000 ppm and 1 in the 500 ppm group. Malignant tumors were observed in 14 animals on 5000 ppm (10 hepatic cell carcinomas, 5 hepatocholangiocarcinomas), in 2 animals on 500 ppm and in 2 controls (all hepatic cell carcinomas). Frequency of hepatic cell adenomas in treated groups (starting at the highest level) was 6, 8, 2, and 1 with 1 also in the control group. One hepatocholangioma occurred in the 5000 ppm group. There was no increase in the frequency of tumors in organs other than the liver. Degree of concomitant liver damage was found to correlate with safrole dose, with severe injury in rats receiving 5000 ppm, and very slight changes at the 100 ppm level. Microscopic alterations included enlargement of hepatic cells (diffuse or nodular), variations in cell size, fatty metamorphosis, architectural irregularity, bile duct proliferation, focal cystic necrosis, focal peripheral margination of cytoplasm, and minimal coagulation necrosis. Other effects of safrole (observed only at 5000 ppm) included a significant increase in mortality (only 2 females and no males out of 50 surviving at 102 days), retardation of growth, mild anemia and leukocytosis, and slight atrophy of the bone marrow. (See also CRA 1(4):#690, 1963.)

63-857 COMPARATIVE SUSCEPTIBILITY OF NEWBORN, WEANLING, AND ADULT MICE TO TUMOR INDUCTION BY 3-METHYLCHOLANTHRENE (3-MC) AND DIBENZO(a,h)ANTHRACENE (DBA). (E., Abstract) O'Gara, R. W. (NCI, Bethesda) and M. G. Kelly. Proc. Am. Assn. Cancer Res. 4(1):49, 1963.

In newborn non-inbred albino mice receiving 20-methylcholanthrene (20-Me; 0.005-11.1 μ g s.c.) or 1,2,5,6-dibenzanthracene (DBA; 0.003-6.7 μ g s.c.) in single inj., mean lung tumor count at 78 wk. was increased at 0.4 μ g of either carcinogen. Subcutaneous fibrosarcomas were obtained with 0.4 μ g 20-Me or with 0.003 μ g DBA. When mice in various age groups up to 8 wk. were given 20-Me (0.00575 mg/g body wt. s.c.) the highest mean lung tumor count at 24 wk. was in mice inj. at 2 wk. of age. On a mg/kg basis the mean tumor nodule count was 2 x that of mice inj. at 1 wk., 6 x that of mice inj. at 0 or 4 wk., and 21 x that of mice inj. at 8 wk. of age.

63-858 PHOTODYNAMIC BIOASSAY OF BENZO(a)PYRENE WITH PARAMECIUM CAUDATUM. (E.) Epstein, S. S. (Lab. Microbiol., Child. Canc. Res. Found., Boston, Mass.), M. Small, J. Koplan, N. Mantel and S. H. Hutner. J. Nat. Cancer Inst. 31(1):163-168, 1963.

A bioassay is described for 3,4-benzpyrene, based on its photodynamic toxicity to *Paramecium caudatum*. (For further details see also CRA 1(2):#192, 1963.)

- 63-859 CONTRIBUTION OF CARCINOGENESIS.
(Ser.) Kosir, A. (Inst. Histol.
Embryol., Ljubljana, Yugoslavia). *Acta Med.
Jugosl.* 16(2):172-180, 1962.

A total of 60 Albany strain mice received urethan (U) in drinking water (no other details); 30/60 were also exposed to 150 r (Cobalt bomb) in a single dose. In the 150 r + U and U only group, on days 270 and 290, resp., lung tumor incidence was 20/29 and 26/30, resp. In irradiated and untreated controls observed at days 482 and 460, resp., tumor incidence was 3/28 and 2/29, resp. Survival was much shorter (no details) among the U-treated animals than in controls; survival of the 150 r + U group was shorter by 20 days compared to the U only group. In the majority of cases, death was not caused by the appearance of lung tumors but rather by severe destruction of liver parenchyma. One benign basophiloma occurred in each of the U-treated groups but none occurred in 60 controls. A total of 6 leukemias, 4 papillomas, and 7 other tumors occurred randomly distributed among the experimental and control animals. The author concludes that U behaves both as a carcinogenic (initiating factor) and as a co-carcinogenic (promoting factor) substance.

- 63-860 ALTERATIONS IN THE FINE STRUCTURE OF HEPATOCYTES PRODUCED BY β -3-THIENYLALANINE. (E.) Hruban, Z. (Dept. Path., U. Chicago, Ill.), H. Swift and R. W. Wissler. *J. Ultrastruct. Res.* 8(3-4):236-250, 1963.

Livers of adult Sprague-Dawley albino rats fed β -3-thienylalanine (β -TA) in phenylalanine-free diets, 2, 3, or 4 x the equimolar replacement of maintenance phenylalanine (111.2-333.6 mg/kg/day x 1-7), showed by light microscopy increased cell volume, enlarged nuclei and nucleoli, and necrotic areas in those fed the highest levels. Cytoplasmic basophilia became diffuse. Ultra-microscopically, the disturbance of protein metabolism induced by the treatment produced the following alterations in the cytoplasmic components of the hepatocytes: disorganization of the rough endoplasmic reticulum; proliferation of smooth endoplasmic reticulum, hyperplasia of the Golgi complex; and a splitting of mitochondrial cristae, such as has been noted in leukemic cells. Large, smooth walled vacuoles were produced, containing small vesicles, often including ribosomes. Some of the ultra-structural changes produced by β -TA resembled those produced by carcinogens, suggesting that these changes may represent nonspecific reactions of the cells to derangement of protein synthesis, rather than an initial stage of carcinogenesis.

- 63-861 DOSE-EFFECT RELATIONSHIP IN CANCER PRODUCTION BY 4-DIMETHYLAMINOSTILBENE IN THE RAT. (Ger.) Druckrey, H. (Surg. Clin., Albert-Ludwigs U., Freiburg/Br., Germany), D. Schmähl and W. Dischler. *Zschr. Krebsforsch.* 65(4):272-288, 1963.

4-Dimethylaminostilbene (DAST) admin. to groups of 30-67 young (3 mo.) BD rats in graded doses from 3.4 to 0.1 mg/kg/day p.o. caused carcinomas of the external auditory canal in all animals which survived long enough. Mathematical analysis showed that the production of cancer is a function of the total dose and that the total dose required decreased with reduction in the daily dose, e.g., with a daily dose of 3.4 mg/kg/day, the average total dose required was 852 mg/kg, whereas with 0.1 mg/kg/day it was only 90 mg/kg. Only the highest dose interfered with normal wt. gain, caused thin hair and poor appearance. With the smallest dose, the rats were heavier than the controls at the same age, but developed typical squamous epithelial cell carcinomas of the ear canal. When 2 mg/kg/day of DAST was given p.o. to black and white spotted rats of strain BD IV, the black spots began to turn white when the total dose reached about 350 mg/kg; this change was irreversible. The average LD₅₀ for adult rats is 70 mg/kg, given as a single dose, i.p. or p.o. In 7 rats, cancers developed simultaneously in other organs: ovary 1, uvea (sarcoma) 3, colon 1, breast 2. Three rats developed only breast cancers and one, monocytic leukemia. When rats of strains BD I, BD III and BD IV were given 2 mg/kg/day, the av. effective total dose producing ear canal carcinomas was 477, 370, and 516 mg/kg, resp., compared to 680 mg/kg for strain BD II. The carcinogenetic effect was irreversible and remained additive over the entire life span of the individual animal.

- 63-862 METABOLIC CHANGES IN RAT LIVER DURING CARCINOGENESIS AND OTHER HEPATIC CONDITIONS. (E., Abstract) Burke, W. T. (W. Va. U. Med. Ctr., Morgantown) and E. C. Gangloff. *Proc. Am. Assn. Cancer Res.* 4(1):9, 1963.

Rats undergoing 3'-methyl DAB or thioacetamide induced carcinogenesis, or were subjected to partial hepatectomy or bile duct-ligation, were examined for extent of tryptophan pyrrolase induction on addition of tryptophan or hydrocortisone in the perfusate used to determine amino acid and protein metabolism (no details). Parameters determined were incorporation of C¹⁴ tryptophan into the liver and plasma proteins, and the expiration of C¹⁴O₂. Compared with the normal response (100%), livers from azo dye fed rats had 100%, from thioacetamide-treated animals 50%, from bile duct cell proliferation 200%, and regenerating livers had 80% capacity for enzyme induction. Livers in the different experimental groups also showed distinct patterns of protein anabolism and catabolism. Thus, although each of these liver types has features in common with the others (e.g. cell proliferation), a unique pattern

enzyme and metabolic activity is found in ch. Such changes may reflect differences in operation of basic control mechanisms.

863 IDENTIFICATION OF THE D-GLUCOSIDES OF STIGMASTEROL, SITOSTEROL AND CAMPESTEROL TOBACCO AND CIGARETTE SMOKE. (E.) Kallianos, G. (Res. Dept., Liggett and Myers Tobacco Co., Ham, N. C.), F. A. Shelburne, R. E. Means, K. Stevens, R. E. Lax and J. D. Mold. Biochem. 87(3):596-600, 1963.

fraction of an uncased commercial blend of tobacco (Burley, Bright, Maryland and Turkish) in light petroleum (b.p. 40-48°) and ethanol, or diethyl ether, water and hexane-extracted condensates from machine-produced cigarette smoke from cased commercial blend flue-cured tobacco, Maryland and Turkish tobaccos contained the same sterol glucosides. The sterol mixture consisted of stigmasterol 60%, sitosterol 25% (probably as the β isomer) and campesterol 15%. Sugar was identified as glucose, and quantitative determination of an aqueous hydrolysate indicated that the isolated material was a glucoside.

864 THE EFFECT OF ADENOSINE TRIPHOSPHATE ON THE TERATOGENIC ACTION OF CORTISONE IN MICE. (E.) Gordon, H. W. (Res. Dept., St. Barnabas Med. Ctr., Newark, N.J.), W. Tkaczyk, A. Peer and W. G. Bernhard. Biol. Neonat. 1(3):340-350, 1963.

CFW females admin. of ATP (0.1-5000 μ g/mouse/day) with cortisone acetate (CA; 2.5 mg/mouse/day) on days 11-14 of gestation caused a significant decrease in the number of pups/mother at 18 days (3.3-6.2 in ATP + CA + CA controls, without relation to ATP dose) compared to ATP-treated mothers (7.3-8.8), buffer controls (BC), or untreated controls (C) 8.4 and 8.9, resp. Gross abnormalities in live fetuses were always accompanied by cleft palate: 3% in BC, 0.3% in UTC, and 0.8-1.0% in ATP-treated controls, without relationship to dose. However, the incidence of cleft palate was very high in CA-treated controls, 94.7%, in 8.5% hydrocephaly, 2.8% deformed spine, absence of eyes, and 0.3% absence of ears. Frequency of cleft palate was high in the ATP + CA-treated group, ranging from 73.4-100%, irrespective of ATP dose. Additional abnormalities were most frequent in the 3 mg ATP + CA group, were more frequent in all groups receiving 500 μ g ATP + CA or more, than in the CA control group. At lower ATP doses the frequency of abnormalities was somewhat decreased with respect to CA controls. While fetal resorptions and deaths were few in the ATP-treated, in BC and UTC, in CA controls there were 34% resorptions and 4.3% deaths in contrast to a 20%-55% frequency of resorptions in the ATP + CA group (highest at 500 μ g ATP + CA) and 5%-20% frequency of fetal deaths (also highest at 500 μ g

ATP + CA). Results seem to indicate that high conc. of ATP enhance the teratogenic effects of CA.

63-865 ACETONITRILE AS A CONSTITUENT OF CIGARETTE SMOKE. (E.) Campbell, J. K. (Southwest Res. Inst., San Antonio, Tex.), J. W. Rhoades and A. L. Gross. Nature (London) 198: 991-992, 1963.

Analysis by gas chromatography of smoke from mechanically smoked cigarettes revealed about 1 mg acetonitrile (methyl cyanide) per cigarette. The compound appears to be a combustion product, since it is not found in unsmoked tobaccos or cigarette paper. The compound has been identified in the body fluids of smokers, and urinary determination has been suggested as a measure of the actual degree of tobacco smoke exposure.

63-866 THE EFFECT OF CIGARETTE SMOKE ON THE RESPIRATORY SYSTEM OF THE RABBIT. A FINAL REPORT. (E.) Holland, R. H. (Dept. Surg., VA Hosp., Dallas, Tex.), E. J. Kozlowski and L. Booker. Cancer 16(5):612-615, 1963.

Exposure of rabbits to "normal" cigarette smoke for 2 to 5½ yr. under rigidly controlled conditions gave the following causes of death in 30 "smokers" and 31 litter mate controls of the same sex, resp.: "snuffles" with pneumonia, 3 and 2; necrobacillosis with septicemia, 4 and 2; anorexia of unknown etiology, 4 and 1; emphysema, 4 and 0; mucoid enteritis, 4 and 4; miscellaneous, 3 and 0; trauma (suffocation in smoking machine and fractured spines), 8 and 1. The nasal passages of controls were normal, those of 7/30 "smokers" showed chronic rhinitis and 3/7 also showed atypical cells in the respiratory epithelium. The pharynx, larynx, and upper tracheas had similar appearances in "smokers" and controls. Of 6 "smoking" rabbits dying during the first yr., 4 exhibited marked proliferation of goblet cells in the main stem, and lobar bronchi. These changes were less frequent in rabbits exposed to smoke for longer periods of time. Cytologic examination of the tracheobronchial mucosa was normal in 7/30 "smokers" and in 21/31 controls. In "smokers" and controls, resp., the following changes were observed: focal hyperplasia, 10 and 6; generalized hyperplasia, 9 and 3; generalized hyperplasia with atypical cells, 3 and 1; and squamous metaplasia, 1 and 0. General emphysema was found in 11/30 "smokers" and in 1/31 controls. Focal emphysema was found in both groups, but appeared earlier in "smokers". The only cancers observed were of the breast, 1 in a "smoker" and 1 in a control.

63-867 INHIBITORY ACTION OF FLAVONOIDS ON MAMMARY CARCINOGENESIS IN THE MOUSE. (Fr.) Rudali, G. (Lab. Genet. Radium Inst., Curie Foundation, Paris) and L. Juliard. C.R. Soc. Biol. (Paris) 157(1):72-74, 1963.

Female RIII mice kept under conditions leading to continuous reproduction had a mammary tumor frequency of 95-90%, starting at 5 mo. of age. Resection of the mammary tumors at the time of their appearance was followed by secondary tumors in 81% of 21, with a mean latency of 73 mo. Treatment from the time of tumor resection with magnesium flavonoid complexes (1.2 mg/day p.o.) or with a lyophilized serum antihyaluronidase preparation (0.1 ml/day i.m. from 1 ampule diluted with 6 ml xylocaine) reduced the frequency of secondary tumors to 20% of 15 and to 25% of 12, resp., with mean latencies of 66 and 101 days. Similar results were obtained on treatment with antihyaluronidase + flavonoid complexes (both admin. i.m.), whereas flavonoid complexes alone had no effect on the frequency or latency of secondary tumors when admin. i.m.

- 63-868 CHEMICAL AND BIOLOGIC TESTING OF THE SMOKE CONDENSATE FROM TOBACCO TREATED BY THE NEUKOMM-BONNET PATENT PROCESS. (Fr.) Cuzin, J. L. (Sci. Commission Coresta, Paris), A. Testa, S. Testa and G. Anguera. *Zschr. Praeventivmed.* 8(2):125-137, 1963.

The effect of a tobacco treatment, claimed by its inventors to reduce about 50% its content of polyaromatic hydrocarbons, was evaluated by analysis of tobacco and smoke condensates; biological effects were tested by skin painting of mice with the smoke condensate. Analysis before smoking of tobacco lots treated (A) by mechanical sprinkling with methylene chloride and untreated (B), showed that the total nicotine alkaloids (A, 1.35%; B, 1.65%) and waxes and resins (A, 3.45 g/100 g; B, 5.04 g) were decreased slightly by the treatment, as was mean weight/cigarette (A, 1.03 g; B, 1.052 g). The smoke condensate per cigarette, from a cigarette smoking machine with a capillary-type smoke trap was decreased slightly in treated tobacco: A, 18.7 mg; B, 19.4 mg. There was no significant decrease in production of hydrocarbons in treated tobaccos (in µg/g of condensate, in A and B, resp.) of anthracene (10.1, 9.8), pyrene (9.4, 8.7), and 3,4-benzpyrene (0.95, 0.91). A more efficient smoking machine, using a liquid air smoke trap, caught more of all 3 hydrocarbons; their content was slightly, but not significantly, higher in the smoke condensates of treated than of untreated tobaccos. Short term skin painting tests of the smoke condensates (at 2 conc.) from treated and from control lots of tobacco, carried out on 4 groups of 120 mice each, with random treatment selection and blind evaluation, showed no significant differences between treated and untreated tobaccos in the resulting disappearance of sebaceous glands nor in cutaneous hyperplasia which indicates early carcinogenesis.

- 63-869 PRECANCEROUS GASTRIC LESIONS IN GUINEA-PIGS AFTER INTRAMURAL INJECTION OF 3-METHYLCHOLANTHRENE. (E.) Zaldivar, R. S. D. (Dept. Biol., U. Chile Sch. Med., Santiago). *Naturwissenschaften* 50(10):380-391, 1963.

Among 20 male and 17 female adult guinea-pigs in with 20-methylcholanthrene (1 mg in 0.05 ml polyethylene glycol-400) into the submucosa (sometimes into the muscular coat, or subserosa) of the ventral wall of the gastric antrum, 14 developed precancerous gastric lesions within 240 days. Among 10 females, one diverticulum was detected after 156 days, and 9 were found at necropsy after 240 days; among the latter was a lesion which infiltrated the epithelium. Among 14 males, 2 diverticula were seen after 106 and 204 days, 5 at necropsy; 2 of the latter were infiltrating epithelial lesions. At necropsy the injection site was detected as a flattened yellow area 1-5 mm in diameter, obscured by local thickening and/or by fibrosis. Many of the treated animals also showed inflammatory and degenerative changes. Most of the infiltrating lesions arose from the blind end of the basal gland in the mucosa, in association with diverticula. In 1 case there was evidence of origin from multicentric neoplastic foci. There were no precancerous or inflammatory changes in 12 controls (6/12 males) inj. with the solvent.

- 63-870 THE QUESTION OF THE PHYSIOLOGICAL ACTIVITY, INCLUDING CARCINOGENICITY OF ALKYLNITROSAMIDES USED IN THE MANUFACTURE OF DIAZOALKANES. (Ger.) Arndt, F. (Inst. Organ. Chem., U. Hamburg, Germany), B. Eistert and W. Walter. *Naturwissenschaften* 50(10):379-380, 1963.

The authors point out the need for a careful evaluation of the physiological and possible carcinogenic properties of all the compounds used as starting materials for the preparation of diazoalkanes, including nitrosomethylurea, nitrosoalkylamides, *N*-(nitrosoalkylamino)-isobutylmethylketone and *N*-(nitrosoalkylamino)-sulfolane, as well as *p*-tosylmethylnitrosamine, which has recently become commercially available.

- 63-871 THE DIFFERENTIAL EFFECT OF LOCALLY AND PARENTERALLY ADMINISTERED ESTROGEN ON THE MUCOSA OF THE VAGINA AND UTERINE CERVIX. (Ger.) Döntenwill, W. (Inst. Path., Ludwig-Maximilians U, Munich, Germany), U. Mohr and J. Bernhard. *Zschr. Krebsforsch.* 65(4):303-308, 1963.

Parenteral diethyldihydroxystilbene dipropionate (Cyren-B; 0.6 mg in oil s.c. every 2 days for 1.5 yr.) had no effect on the vaginal or uterine mucosa of female golden hamsters. However, when suppositories containing 40 mg of this estrogen were implanted in the upper vagina of golden hamsters every 8 wk. for 1 yr., beginning at the age of 6 wk., even those dying in the first 10 mo. showed mild to moderate epithelial proliferation and inflammatory infiltration, and 6/9 animals which survived 14-16 mo. showed squamous cell carcinoma of the vagina or uterine cervix. Mechanical irritation may, however, have played a role in these changes.

872 FURTHER STUDIES ON THE CARCINOGENIC AND GROWTH-INHIBITORY ACTIVITY OF LACTONES AND RELATED SUBSTANCES. (E.) Dickens, (Middlesex Hosp. Sch. Med., London, W.1) and E. H. Jones. Brit. J. Cancer 17(1):100-108, 1963.

The number of rats alive with local tumors following s.c. admin. to male rats of penicillid (PA; 0.1 mg x 2/wk. x 61 wk. in arachis oil) was 1/4; PA (2 mg x 2/wk. x 52 wk. in water), 1/4; maleic anhydride (MA; 1 mg x 2/wk. x 61 wk.), 1/4; $\beta\beta$ -dimethyltrimethylene oxide (DO; 1 mg x 2/wk. x 51 wk.), 2/4; penicillin G (PG; 2 mg x 2/wk. x 65 wk.), 5/11; and parasorbic acid (PSA; 2 mg x 2/wk. x 32 wk.), 4/6; and PSA (2 mg x 2/wk. x 32 wk.), 4/5; compared with controls, 5 ml arachis oil), 0/4, when rats were observed 95-106 wk. after treatment. Compounds with the reactive ring structure such as hydroxy-pionic acid and sodium maleate did not induce tumors. The time (in wk.) at which tumors first appeared was, for PA in oil, 94; PA in water, 56; MA, 80; DO, 83; PG, 78; and PSA, 63. PG induced malignant transplantable sarcomas and PA (in water) induced highly malignant tumors with invasive properties and high degree of autonomy on transplantation, while MA and DO induced sarcomas and fibrosarcomas, some of which were malignant and almost all of which were transplantable. Remote, spontaneous tumors were found in rats which did not develop tumors at the site of inj. One treated rat developed a testicular tumor on the side in which the inj. was made; this was the only testicular tumor found in the rat group. This paper also deals with the growth inhibitory activity of lactones and related substances.

873 FACTORS INFLUENCING ESTROGEN-INDUCED MAMMARY TUMORS IN THE RAT. (E., abstract) Cutts, J. H. (Cancer Res. Inst., U. of Western Ontario, London, Canada). Proc. Am. Cancer Res. 4(1):13, 1963.

One or diethylstilbestrol pellets were implanted in the backs of hooded-strain rats. Additional estrogens or other hormones (testosterone, progesterone, growth hormone) were administered during the latent period, or after tumor development. Ovariectomy, adrenalectomy, or hypophysectomy was performed before implantation or after tumors had appeared. Nine to 16 months after the initial implant, 90% of animals developed multiple mammary tumors. A few were fibroadenomas but most were carcinomas which showed local invasion and lymphatic or pulmonary metastases. Tumors regressed on removal of the estrogen pellet but reappeared on repelleting. Repelleting involved mainly resurgence of previous tumors, but new tumors also appeared. Tumor resurgence occurred rapidly even if repelleting was delayed 6 wk. Multiple pellets, or inj. of additional estrogen reduced the period for tumor induction, but did not alter the course of

established tumors. Testosterone, progesterone or growth hormone increased the latent period, and caused temporary regression of tumors. Ovariectomy and adrenalectomy likewise prolonged the latent period and temporarily reduced tumor size. No tumors occurred in hypophysectomized animals, and such treatment induced permanent regression of established tumors.

63-874 THE INFLUENCE OF PSEUDOPREGNANCY ON BREAST TUMOUR INDUCTION IN C57B1 MICE BY VARIOUS CHEMICAL CARCINOGENS. (E.) Marchant, J. (Dept. Path., U. Birmingham, England). Brit. J. Cancer 17(1):119-126, 1963.

Intact and pseudopregnant adult female C57B1 mice received approx. 2.5 mg topically of one of the following every 2 wk. x 6-8: 9,10-dimethyl-1,2-benzanthracene (DMBA); 20-methylcholanthrene (20-Me); dibenzanthracene (DBA); or benzpyrene (BP). In virgin and pseudopregnant mice, after BP, the incidence of breast tumors was, resp.: 0/16 and 0/18; after DBA, 24% of 17 and 14% of 14; after DMBA, 7% of 14 and 72% of 29. In virgin and pseudopregnant mice, incidence of ovarian tumors after DBA was 6% of 17 and 0% of 14; after DMBA 7% of 14 and 14% of 29; none occurred after BP. Incidence of skin tumors was, after BP, 50% of 16 and 33% of 18; after DBA, 7% of 17 and 14% of 14; after DMBA, 43% of 14 and 17% of 29. Among 18 mice made pseudopregnant after completion of treatment with 20-Me, incidence of breast, ovary and skin tumors was 17%, 0% and 56%, resp. In pseudopregnant mice the onset of tumors occurred at 6 wk. for DMBA; 14 for 20-Me; and 64 for DBA. There appeared to be no correlation of tumor type with carcinogen used. In DMBA-treated pseudopregnant mice, earliest tumors were squamous, the later ones glandular. The higher incidence among some virgin groups is possibly related to their longer survival.

63-875 THE INDUCTION OF AMINOAZO DYE N-DEMETHYLASE IN NONHEPATIC TISSUES BY 3-METHYLCHOLANTHRENE. (E.) Gilman, A. G. (Dept. Pharmacol., Western Reserve U. Sch. Med., Cleveland, Ohio) and A. H. Conney. Biochem. Pharmacol. 12(6):591-593, 1963.

Male Sprague-Dawley rats treated with 20-methylcholanthrene (1 mg/d x 2 i.p. in corn oil) markedly increased N-demethylase activity in microsomes of lung, kidney and liver (729, 425 and 234%, resp., compared to microsomes from normal tissue); microsomes of brain or testis were not stimulated. In treated rats enzyme activity (expressed as μ g 3-methyl-4-aminoazobenzene formed oxidatively from 3-methyl-4-monomethylaminoazobenzene) was 49.6 for microsomes from 133 mg liver incubated 12 min., and 0.8, 0.5, 9.9 and 2.1 for microsomes from 13.3 g brain, 4.0 g testis, 4.0 g lung and 6.0 g kidney incubated 60 min. Phenobarbital (37.5 mg/kg x 2/day x 4 i.p.) stimulated N-demethylation in liver, but not in extrahepatic microsomal systems. Results expand previous findings of

drug-stimulated (polycyclic hydrocarbons, pheno-barbital, aminopyrene, phenylbutazone, orphenadrine) N-demethylase activity in liver microsomes to other organs concerned with drug detoxification, suggesting that the pharmacologic action of some drugs may be altered in animals receiving these types of compounds.

- 63-876 **AUTORADIOGRAPHY AND ENZYMATIC DISSECTION OF MOUSE SKIN FOLLOWING APPLICATION OF TRITIATED POLYCYCLIC HYDROCARBONS.** (E., Abstract) Giovanella, B. C. (McArdle Memorial Lab., U. Wisconsin, Madison) and C. Heidelberger. Proc. Am. Assn. Cancer Res. 4(1):23, 1963.

The backs of Swiss albino mice were painted with 9,10-dimethyl-1,2,5,6-dibenzanthracene- H^3 and 1,2,3,4-dibenzanthracene- H^3 (130 μC in 0.1 ml benzene, 2 x/wk. x 1, 2 or 3 wk.) and sectioned skins were examined by autoradiography. The autoradiographs showed an accumulation of radioactivity in the keratinized layer and in the pilosebaceous apparatus, with stronger labeling from the carcinogenic hydrocarbon in the epithelial cells.

- 63-877 **AN EFFECT OF 3-METHYLCHOLANTHRENE (MC) TREATMENT ON THE PROTEIN SYNTHETIC APPARATUS OF RAT LIVER.** (E., Abstract) Gelboin, H. V. (NCI, Bethesda) and L. Loeb. Proc. Am. Assn. Cancer Res. 4(1):22, 1963.

A liver microsomal system from 20-methylcholanthrene (20-Me) treated rats incorporates 50% more amino acids than normal liver preparations. Both systems are puromycin and RNase sensitive. The 20-Me effect was observed when sRNA-amino acid was used instead of free amino acids, when microsomes freed of messenger RNA (mRNA) were allowed to incorporate L-phenylalanine- $U-C^{14}$ in the presence of excess polyuridylic acid, and also in the same system, but with added saturating levels of normal microsomes freed of mRNA, and thus rendered mRNA limited. Results are interpreted as due to an increase in the amount of mRNA available in the microsomes of 20-Me treated animals.

- 63-878 **CHARACTERISTICS OF MAMMARY CANCER INDUCED BY IRRADIATION OR 7,12-DIMETHYLBENZ(a)ANTHRACENE.** (E., Abstract) Fukunishi, R. (Ben May Lab. Cancer Res., U. Chicago, Chicago, Ill.) and C. Huggins. Proc. Am. Assn. Cancer Res. 4(1):21, 1963.

Mammary cancers induced in Sprague-Dawley female rats by a single feeding of 9,10-dimethyl-1,2-benzanthracene (DMBA) or by a single total-body irradiation (400 r) at age 50 days showed a similar histologic picture, similar content of 6 pyridine nucleotide linked dehydrogenases, and similar regression after oophorectomy. Period of observation was 180 days. Irradiation induced 30% mammary

cancers, 16% fibroadenomas, and 4% sarcomas. DMBA treatment induced 100% mammary cancers, 89% fibroadenomas, 5% ear duct tumors, and 2% leukemias.

- 63-879 **EFFECT OF A LIVER EXTRACT ON THE FORMATION OF HEPATOMAS IN RATS FED BUTTER YELLOW.** (Ger.) Heise, E. (Robert-Rössle-Clin., German Acad. Sci., Berlin) and M. Görlich. Exp. Cell Res. 30(3):583-587, 1963.

When 60 adult female inbred white rats were fed dimethylaminoazobenzene (DAB; 5 mg/day x >200), 10/20 developed hepatomas. After additional therapy with fructose-1,6-diphosphatase (FDPase; prepared from the cytoplasm of beef liver homogenate, 1 ml i.m. x 2/day, absolute activity 30 U/ml) throughout the experimental period of 280 days or starting 2 mo. after initiation of DAB, 15% of 40 rats developed hepatomas. A control series given only FDPase (3 ml/day), all survived without anaphylactic shock; therefore, the few early deaths in all 3 DAB groups were attributable to the carcinogen. The activity of FDPase activity in hepatoma homogenates was 57.6 U/ml, while in normal rat liver homogenates it was 94.3 U/ml; thus, the enzyme significantly reduced tumor cell glycolysis. While carcinogen in DAB-fed rats was significantly decreased by FDPase admin., and was inversely proportional to the absolute activity of the FDPase in the tumor, no dependence on the specific activity could be demonstrated. (For earlier studies, see CRA 1(4):#652, 1963.)

- 63-880 **MODE OF FORMATION OF 3,4-BENZOPYRENE AT HIGH TEMPERATURES.** (E.) Badger, G. M. (U. Adelaide, S. Australia) and J. Novotny. Nature (London) 198:1086, 1963.

It was previously felt, and subsequently confirmed that 3,4 benzpyrene is formed by high temperature reactions from simpler hydrocarbons, and that a C_6-C_4 compound may be the critical intermediate. Pyrolyses of butylbenzene, tetralin and n-decane at 700° have given tars containing significant amounts of 3,4-benzpyrene. Two molecules of a compound such as butylbenzene combine with each other, and subsequently undergo cyclodehydrogenation to form 3,4-benzpyrene.

- 63-881 **NUCLEOLAR CHANGES INDUCED BY IONIZING RADIATIONS AND CARCINOGENIC AGENTS.** (Abstract) Montgomery, P. O'B. (U. Texas Southwestern Sch. Med., Dallas, Texas), R. C. Reynolds, D. Karney and B. Hughes. Fed. Proc. 22(2):315, 1963.

Chang liver cells in tissue culture were exposed to ionizing radiation (600 r), actinomycin D, or nitrogen mustard for 20, 50 or 150 hr. Ionizing radiation produced nucleolar fragmentation, enlargement, and nucleolar "doughnuts". Actinomycin D produced nucleolar changes identical to those

used by 4-nitroquinoline-N-oxide (see CRA
#451, 1963) which consisted of nucleolar
destruction, nucleolar fusion, and the development
of a "nucleolar cap". Nitrogen mustard produced
nucleolar changes.

882 ROLE OF THE ADRENAL IN HEPATIC
CARCINOGENESIS. (E., Abstract)
Herber, M. D. (Beth Israel Hosp. and Harvard
Med., Boston, Mass.). Fed. Proc. 22(2):
1963.

Hepatomas induced in male F1 hybrid rats (male
x female Sprague-Dawley) fed N-2-fluorenyl-
acetamide (0.025%, in a semisynthetic diet)
were not prevented by adrenalectomy (ADX).
However, in ADX males hepatoma formation was
prevented by deoxycorticosterone, 9- α -fluoro-
corticosterone, testosterone or norethandrolone,
by castration + cortisone admin. In intact
males, adrenocorticotropin (but not deoxy-
corticosterone, or 9- α -fluorodeoxycorticosterone),
increased the frequency of hepatomas. 6 α -
methylprednisolone (Medrol) did not decrease the
frequency of hepatomas in intact or ADX males.
Intact or ADX females given cortisone, 9- α -fluoro-
corticosterone, or no hormone treatment, did not
develop hepatomas. Results indicate that ADX alone
does not prevent development of hepatomas in
these rats, although hepatomas are prevented by
administration of mineralocorticoids to ADX animals, or
removal of anabolic hormones by ADX +
castration.

883 STUDIES ON THE METABOLISM OF N-HYDROXY-
2-ACETYLAMINOFLUORENE-9-C¹⁴ BY RABBIT-
LIVER CELL FRACTIONS. (E., Abstract) Irving,
J. (Dept. Biochem., U. Tennessee Med. Units,
Knox, Tenn.). Proc. Am. Assn. Cancer Res. 4(1):30,
1963.

Rabbit liver 10,000 x g supernatants, 95% of
the N-hydroxy-acetylaminofluorene-9-C¹⁴ (N-
hydroxy-AAF) disappeared under hydroxylating
conditions in 30 min. at 38°C. After extraction
of the incubation mixture with ether, 40%-60%
of the radioactivity remained in the aqueous
phase indicating a product other than N-hydroxy-
AAF. When the ether-extracted aqueous phase
was treated with β -glucuronidase, however, the
major portion of the water-soluble metabolite(s)
was extractable in ether and recoverable as
N-hydroxy-AAF. In rabbit liver microsomes,
however, only 35% of the added labeled N-hydroxy-
AAF disappeared in 30 min., and all of the radio-
activity was recoverable in the ether fraction.
The disappearance of N-hydroxy-AAF in the micro-
somal system was inhibited by 0.1 M sodium
fluoride.

884 EFFECTS OF SUBCUTANEOUS INJECTION
OF DIETHYLNITROSAMINE IN THE SYRIAN
HAMSTER. (E., Abstract) Herrold, K. McD. (NCI,
Bethesda) and L. J. Dunham. Proc. Am. Assn.
Cancer Res. 4(1):28, 1963.

Syrian hamsters inj. with diethylnitrosamine
(2 x/wk. x 3-6 mo. s.c.) and surviving more than
4 mo. developed squamous cell papillomas of the
trachea, bronchi and bronchioles, tumors of both
regions of the nasal cavity, and hepatocellular
carcinomas. Induction of tumors of the tracheo-
bronchial tree and nasal cavity by the s.c. route
indicates that the inhalation route is not neces-
sarily the principal portal for induction of
bronchogenic neoplasms.

63-885 STUDIES ON THE MECHANISM OF INITIATION
OF OVARIAN TUMOURS IN MICE BY 9:10-
DIMETHYL-1:2-BENZANTHRACENE (DMBA). (E., Abstract)
Jull, J. W. (Cancer Res. Ctr., U. British Columbia,
Vancouver, Canada). Proc. Am. Assn. Cancer Res.
4(1):32, 1963.

Ovaries from C57/1F mice treated once with 9,10-
dimethyl-1,2-benzanthracene (DMBA; 5 mg in oil
p.o.) and transplanted 24 hr. later to concurrent-
ly ovariectomized recipients developed ovarian
tumors in 50% of the transplants. Injection
during the period of carcinogen application of 11-
deoxycorticosterone (but not of progesterone or
testosterone), suppressed tumor formation com-
pletely. Vaginal keratinization at 10 wk. was
increased to 50-80% in animals which developed
tumors, but remained 20-30% for normal ovarian
transplants and those receiving DMBA + 11-deoxy-
corticosterone. It is suggested that 11-deoxy-
corticosterone or its metabolites and DMBA com-
pete for the same tissue receptors.

63-886 INVESTIGATIONS OF THE MUTAGENIC ACTION
OF NITROSAMINES AND OF NITROSOMETHYL-
UREA. (Ger.) Pasternak, L. (Inst. Exp. Cancer
Res., German Acad. Sci. Berlin, Berlin-Buch).
Acta Biol. Med. Germ. 10(3-4):436-439, 1963.

Diethylnitrosamine (DENA), ethyl-t-butyl nitrosamine
(EBNA) and nitrosomethylurea (NMU) were fed to
Drosophila melanogaster in solution in sugar water
and studied for their effect on the rate of re-
cessive lethal mutations of the X-chromosome by
the M-5-Test. The carcinogenic compound DENA
produced an increasing rise of the mutation rate
with increasing numbers of days following treat-
ment, which reached a maximum of 8.1% 12-15 days
after drug admin. At equal conc., the mutation
rate following NMU admin. was higher than that
produced by DENA, but a marked sterilizing effect
took place. Experiments with EBNA failed to show
any increase of the mutation rate (as compared to
the controls) and any carcinogenic effect. The
parallelism of mutagenic and carcinogenic activity
is explained on the basis of the alkylation
mechanism.

63-887 SKIN TUMOR PROMOTION BY TOPICAL
APPLICATION OF ANTHRACIN (1,8,9-
ANTHRACEN-10-OL). (E., Abstract) Yashuhira, K.
(New York State Health Dept., Springville)
and F. G. Bock. Proc. Am. Assn. Cancer Res.
4(1):74, 1963.

In mice, after initiation with urethan (i.p.), anthralin (0.033%) was a less potent skin tumor promoter than croton oil (0.1%). The first tumors from croton oil appeared at 7 wk. and tumor development was rapid; whereas tumors from anthralin did not appear until 10 wk. and grew more slowly.

63-888 N-HYDROXY ACETYL AMINO COMPOUNDS, URINARY METABOLITES OF AROMATIC AMINES IN MAN. (E., Abstract) Troll, W., S. Belman and E. Rinde. Proc. Am. Assn. Cancer Res. 4(1): 68, 1963.

A new micromethod for quantitative assay of N-hydroxyacetyl amino compounds in the urine based on chelation of the cupric ion gave satisfactory recoveries for N-hydroxy-N-2-fluorenylacetamide and N-hydroxy-N-2-naphthylacetamide. In pts. admin. 200 mg benzidine, 6/6 excreted an acetyl-N-hydroxy compound; after 600 mg 2-naphthylamine, only 2/5 pts. excreted N-hydroxy-2-naphthylacetamide. Normal urine did not contain copper chelating material.

63-889 ON THE CARCINOGENICITY OF CHOLESTERIN AND OF ITS 5 AND 7 HYDROPEROXIDES. (It., Abstract) Koch, R. (Radiol. Inst., Albert-Ludwigs U., Freiburg/Br., Germany). Minerva Med. 54(38):1404, 1963.

Rats after total body irradiation (600 r) and treatment with cholesterol (cholesterin) or its 5-hydroperoxide, the tumor frequency at 2 yr. was 17.4% and 9.5%, resp. In mice with a spontaneous tumor frequency in females of 10.2%, treatment with cholesterol or its 7-hydroperoxide had no effect on tumor frequency (about 10%); however, admin. of the 5-hydroperoxide raised the tumor frequency to 34.9%. In both rats and mice carcinogenic action was not pure and the tumors observed showed a wide variety of types, with no preponderance of any specific tumor type.

63-890 THE CARCINOGENIC ACTION OF $\Delta^3,5$ -CHOLESTADIENE. (Ger.) Schubert, K. (Germ. Acad. Sci. Berlin) and W. Fischer. Arch. Geschwulstforsch. 20(3):177-179, 1963.

A series of 50 white mice (Agnes-Bluhm strain) and 50 black mice (C57) received a single s.c. dose of $\Delta^3,5$ -cholestadiene, (20 mg in sesame oil) into the cervical region. Among 13 white and 6 black mice which died within 10 mo., 3 white mice had histologically confirmed tumors (2 mammary adenomas and one mammary carcinoma with pulmonary metastases). None of the 6 black mice showed any tumor. The white mice, at the site inj., exhibited one case of fibroma, one papilloma, 3 cases of fibrosarcoma and one of adenocarcinoma; the black mice yielded one fibrosarcoma and one carcinoma. In addition, 36 malignancies of various types were present in the white mice, and 35 in the black mice. Detailed comparison of the two groups revealed higher incidence of adenomas and adenocarcinoma in the lungs of the black mice, and a higher incidence of mammary adenocarcinomas in the white mice. Of 20 white mice with tumors, 6 had multiple growths, compared to 2/22 among the black mice. Altogether, 3 cases of sarcomas of reticuloendothelial origin were encountered. No controls were detailed.

63-891 ENTRY AND LOCALIZATION OF BENZO(A)-PYRENE IN TISSUE CULTURE AND THE PHOTOTOXIC RESPONSE OF EXPOSED CELLS TO ULTRAVIOLET RADIATION. (E., Abstract) Morimura, Y. (NCI, Bethesda), H. L. Falk and P. Kotin. Proc. Am. Assn. Cancer Res. 4(1):45, 1963.

Benzpyrene (BP) dissolved in nutrient medium entered very rapidly into HeLa, M5 and human amnion cells, where it became localized in the cytoplasm. Within a few minutes after exposure to UV light in the presence, but not in the absence of oxygen the UV fluorescence caused by the compound disappeared. Cells previously exposed to BP lost most of the carcinogen on repeated washings with the nutrient medium containing protein. Exposure of cells containing BP in high conc. to UV led to cell death, characterized by cytoplasmic blebbing, followed by cytoplasmic and nuclear degeneration. On prolonged exposure of the cells to UV irradiation, cytoplasmic and nuclear alterations were of a different type. The cytopathogenic effects were a function of the BP incorporated into cells and of the energy of the UV dose. Washed cells showed a low order of toxicity.

See also abstract nos.: 781,796,804,816,817, 928,999,1000

VIRAL CARCINOGENESIS

892 MICROSPECTROPHOTOMETRIC STUDIES OF DEOXYRIBONUCLEIC ACID CONTENT OF MURINE LYMPHOMA CELLS (STRAIN P388 D₁) INFECTED WITH POLYOMA VIRUS. (E.) Rabotti, G. (Dept. Path., Jefferson Med. Coll., Philadelphia), A. S. Mason and R. A. Malmgren. *J. Nat. Cancer Inst.* 19(6):1095-1101, 1963.

Microspectrophotometric studies of DNA in Feulgen preparations from cultures of murine lymphoma cells (strain P388 D₁) infected with 107.5 TCID₅₀ polyoma virus revealed no increase in nuclear DNA-Feulgen complex or in nuclear volumes 24 hr. after infection, when viral growth or cytopathic effects were not apparent. Increased nuclear DNA content and nuclear volume were observed 48 and 72 hr. after infection when cytopathic effects were evident and viral growth had commenced.

893 TRANSFORMATION OF CULTURES OF HUMAN ORAL TISSUE INFECTED WITH SIMIAN VIRUS SV40. (E.) Koprowski, H. (Harrison Dept. Res. Surg., University of Pennsylvania Sch. Med., Philadelphia), J. H. J. ten, F. Jensen, R. G. Ravdin, P. Moorehead and E. Saksela. *Acta Un. Int. Cancr.* 19(1-2):1-367, 1963.

Simian virus (SV40) was recovered 96 days after infection of human buccal mucosa and skin collected by biopsy were infected with SV40; 1 skin specimen contained a virus conc. of 103.5 TCID₅₀/ml on day 28 after infection. Transformation occurred 8-14 days after exposure in 5/5 series of buccal mucosa cultures and 2/2 skin cultures as evidenced by tight linear packing of cells (with a cell density of 2-3x normal), numerous mitoses, nuclear appearance of cells, increasing proportion of altered cells, epithelial-like growth, acid fastness in cultures, polymorphism, and nuclear abnormalities. No transformation occurred in infected control cultures. Chromosomal aberrations including dicentric, monosomic, and subcentric chromosomes, rearrangements and subclonal populations were found in hypotetraploid cells.

894 EARLY DETECTION AND LOCALIZATION OF SWISS MOUSE LEUKEMIA VIRUS. (E.) Friend, C. (Dept. Microbiol., Cornell U. Med. Coll., New York) and C. Friend. *Acta Un. Int. Cancr.* 19(1-2):348-350, 1963.

Development of Friend leukemia virus development by immunofluorescence in Swiss mice revealed that the virus appears in the nuclear and perinuclear areas of single liver cells or small groups of cells 5-7 days after infection with filtrates of 20% infected spleen cell suspensions. Later the antigen was found in the cytoplasm; subsequently larger foci of cells were infected. After day 14, no antigen was found in the nuclear area. Virus titers increased concomitantly in livers and spleens,

where virus was infectious starting on day 5 and leveling on days 10-12. Immune sera had low levels of neutralizing antibodies and hemagglutination inhibition was used to evaluate sera.

63-895 STUDIES ON SEVERAL LINES OF MURINE LYMPHOMAS ASSOCIATED WITH INTRACYTOPASMIC PARTICLES. (E.) Friend, C. (Sloan-Kettering Inst. Cancer Res., New York), E. De Harven and J. Haddad. *Acta Un. Int. Cancr.* 19(1-2):344-347, 1963.

Electron microscopic studies of spontaneous lymphoma tissue in Swiss mice (frequency 6.7%) revealed intracytoplasmic particles (LP) consisting of 2 concentric membranes never within the nucleus or outside of the cell in 68.7% of the samples examined. Larger extracellular particles were found in 21.3% of the samples and may have resulted from LP extrusion. Staining reactions (immunofluorescence method using anti-nuclear sera or acridine orange staining) indicated that LP contain nucleoprotein of the DNA type. Lymphomas of Swiss mouse origin grafted to adult DBA/2 mice produced histologically identical disease after a latent period of several mo.; tumors were 100% transplantable to DBA/2 mice but not to Swiss mice, indicating that the tumor cells are of DBA/2 origin. LP were found in DBA/2 lymphomas but not in a different DBA/2 solid leukemic tumor. Since DBA/2 mice do not develop spontaneous leukemia, it is suggested that a malignant transformation of the lymphocytic system of DBA/2 mice may have been mediated by LP present in the Swiss mouse inoculum. The cell suspensions of the 14th passage of a lymphoma passaged in DBA/2 mice produced lymphomas in 10/10 DBA/2 mice in 2 wk. and in 3/10 Swiss mice in 8 mo.; the cell-free filtrate of this material produced lymphomas in 4/10 DBA/2 mice and in 5/10 Swiss mice in 5 mo.; the X-irradiated cell suspension (6,000 r) produced lymphomas in 6/10 DBA/2 mice in 1 mo. and in 6/10 Swiss mice in 3 mo.

63-896 VIRUSES AND CANCER. (E.) Friend, C. (Sloan-Kettering Inst. Cancer Res., New York). *Acta Un. Int. Cancr.* 19(1-2):239-242, 1963.

When tumors of Swiss mice with virus-induced Friend's leukemia were serially passaged in DBA/2 mice immunized with formalin inactivated virus, little or no virus was isolated from tumors or spleens. However, after a number of successive passages when the tumor was returned to unimmunized mice, virus was again recoverable from tumors and spleen even after 35 passages in vaccinated mice. Histologically the tumors of immunized mice were similar to those of untreated mice but the spleens of the former were normal and free of the characteristic cells of the virus-induced leukemia. Since the vaccinated mice did

not develop generalized leukemia, the tumors appear to be autonomous. The author suggests that extracellular virus may be neutralized by antibodies directed against it in immunized mice and is unable to spread to other organs but is able to propagate itself. A second possibility is that the virus in immunized mice is maintained in an incomplete form unaffected by antibodies. Offspring of the cross (C57BL virus resistant females x DBA/2 virus sensitive males, designated BDF₁) survived several repeated inoc. with virus; s.c. tumor grafts grew progressively although spleen and liver remained normal. Little virus was isolated from the tissues of these hybrid mice but virus was recovered after a further passage in infant Swiss mice.

- 63-897 COMPARATIVE STUDY OF THE REACTIVE SURFACES OF POLYOMA AND INFLUENZA VIRUSES. (E.) Ackermann, W. (Dept. Epidemiol., U. Michigan, Ann Arbor). Acta Un. Int. Cancr. 19(1-2):324-327, 1963.

Polyoma viruses like the myxoviruses agglutinate RBC and are isoreceptive in the reaction with PR-8 strain of influenza virus: prior adsorption of increasing conc. of PR-8 reduces the capacity of cells to adsorb polyoma virus and the adsorption of 6000 units or more will completely exclude the adsorption of any detectable polyoma virus. Adsorption of increasing conc. of polyoma virus onto cells also reduces the amount of PR-8 virus that can be adsorbed, however, maximum adsorption to cells of polyoma virus does not completely exclude the uptake of PR-8. The similarity of the 2 viruses in their reactivity with RBC receptors and with a mucoprotein isolated from bovine serum is not shared with regard to the host cell (primary mouse embryo) since here polyoma receptors, unlike PR-8 receptors, are neuraminidase insensitive. Further, a fraction (unspecified) of bovine serum can block the initiation of polyoma, but not of PR-8 infection. The fraction is heat, formol and neuraminidase resistant.

- 63-898 STUDIES OF THE INTERACTION BETWEEN POLYOMA VIRUS AND ITS HOST ANIMALS. (E.) Sjögren, H. O. (Inst. Tumor. Biol., Karolinska Inst., Stockholm). Acta Un. Int. Cancr. 19(1-2):330-331, 1963.

Pretreatment of adult male mice with polyoma virus induced a state of resistance against subsequent transplantation of isologous polyoma tumors (PT) but not to tumors induced by other means. Resistance was overcome by increasing the number of cells in the test challenge. Virus-treated recipients were resistant to 39/43 PT of different morphology, including s.c. sarcomas, thymomas, osteogenic sarcomas, hemangiomas, and epithelial skin tumors and 1 *in vitro*-induced PT. Similar resistance was observed in 1 methylcholanthrene-induced

sarcoma and 1 spontaneous mammary carcinoma among 31 non-polyoma induced tumors tested; the other 29 grew equally well in experimental and control mice. Mice pretreated with PT originating in a mouse of foreign genotype were resistant to isologous PT but not to isologous methylcholanthrene induced or spontaneous mammary tumors; those given non-PT induced tumors of foreign genotype also developed no resistance. Since only recipients without antiviral antibodies were tested, it is concluded that resistance was induced by cellular antigens peculiar to PT and shared by all or most PT. Virus inoc. subsequent to 400 r total body irradiation of recipients induced no resistance; irradiation 5 days after viral inoc. did not abolish induction of resistance. Lymph nodes and spleen cells of virus-pretreated animals neutralized PT cells after the two were mixed *in vitro* and inoc. into compatible mice.

- 63-899 ATTEMPTS TO IDENTIFY HUMAN TUMOUR VIRUSES. (E.) Trentin, J. J. (Div. Exp. Biol., Baylor U. Coll. Med., Houston, Texas), Y. Yabe and G. Taylor. Acta Un. Int. Cancr. 19(1-2):271-272, 1963.

Of 9 human adenoviruses tested, only type 12 undifferentiated sarcomas (Ad-12) produced tumors, all of which were at the site of intrapulmonary inj. in 9/11 hamsters in 90 days. Inj. of cell-free filtrates of Ad-12, subpassaged 1-8 x in HeLa cells, also produced a high incidence of tumors. In 1 infected hamster, several histologically undifferentiated sarcomas developed, in addition to intrapulmonary tumors. Tumors, serially transplantable into unconditioned young adult hamsters were also produced by i.p. inj. of Ad-12. The Ad-12 preparation was free of polyoma virus, as shown by the induction of a different type of tumor primarily at the site of inj., by the ready propagation in HeLa cells, and by the absence of polyoma hemagglutination inhibiting antibodies in infected animals. Contamination by SV40 was ruled out by the absence of typical vacuolation in cercopithecus kidney, by its sensitivity to heat inactivation at 60 C for 30 min., and by insensitivity to treatment with anti-SV40 antiserum. Electron microscopy of Ad-12 infected HeLa cells revealed a typical adenovirus. Some 26% of 700 randomly selected hospital pts. had sera neutralizing Ad-12 at dilution of 1:4 or higher. Seven such positive and 4 negative sera were negative for SV40 antibodies although 4 of the positive sera neutralized cytopathogenic effects on HeLa cells due to Ad-12, whereas the 4 negative sera did not.

- 63-900 FAILURE TO DETECT VIRUS IN HAMSTER TUMORS INDUCED BY HUMAN ADENOVIRUS TYPE 12. (E., Abstract.) Trentin, J. J. (Div. Exp. Biol., Baylor U. Coll. Med., Houston, Texas), Y. Yabe and G. Taylor. Proc. Am. Assn. Cancer Res. 4(1):68, 1963.

empts at the demonstration of human adenovirus 12 (Ad-12) in hamster lung, or in the local comas induced by Ad-12 inj. in hamsters were negative. Included were: a search for the pathogenic viral particles known to be present in infected HeLa cell cultures, inoc. of HeLa cultures with homogenates of 6 primary transplanted Ad-12-induced hamster tumors, of the fluid from primary cultures of the tumors, and inoc. of homogenized lung from 8-day-old hamsters inj. at birth with Ad-12. In hamsters with primary tumors induced by Ad-12 inj. at birth 5/12 were positive for Ad-12 antibodies, no antibodies could be detected at 14-42 days in adult hamsters inoc. with 5 of the positive and 1 negative tumor.

901 CYSTS IN MICE INDUCED WITH EXTRACTS OF LUNG TISSUE FROM CASES OF SHEEP PULMONARY ADENOMATOSIS SIMILAR TO CYSTS CAUSED BY SARCOMA VIRUS IN RATS. (E.) Shapiro, S. (Gamaleya Inst., Moscow), A. M. Gardachyan, M. Mitrofanov and L. A. Zilber. Acta Un. Int. 19(1-2):290-293, 1963.

Born mice of the C57Bl and CC57Br strains inoc. with material from sheep pulmonary adenomatosis developed cysts with about equal frequency 7/22 receiving filtrates (frozen or glycerol treated), in 3/3 receiving homogenate sediments, 4/10 receiving supernatants from 1000 g wash, frozen, or glycerol treated), and in 3/3 receiving supernatants from 4500 g wash, frozen, or glycerol treated). Upon histological examination it was seen that the cyst formation was the result of proliferative and destructive changes in lymph nodes and ensuing hyperplasia and fusion of sinuses. No cysts developed in mice of the A, CC57W, or C3H strains inoc. with the same materials, or in susceptible mice receiving material inactivated at 65°C for 60 min. A reticulum cell sarcoma was observed adjacent to a cyst in a C57Bl mouse 5 mo., and microscopic sarcomatous changes were found near the cyst wall of a CC57Br mouse. Mixture of extracts from cyst wall and cyst contents, and of liver, spleen, kidney, and lymph nodes of affected animals caused cysts in 23/45 surviving 5 mo., although inoc. of cyst contents alone was ineffective. On second passage (still in progress), 4/23 mice have developed cysts at 3 mo. The frequency of spontaneous cysts in the 2 susceptible mouse strains ranged from 1.5-2.0%.

902 STUDIES ON THE BEHAVIOR OF THE BITTNER VIRUS IN MICE OF SOME APPARENTLY VIRUS-SUSCEPTIBLE STRAINS. (E.) Dmochowski, L. (U. Texas A. & M. Anderson Hosp., Houston), C. E. Grey and J. Sykes. Acta Un. Int. Cancr. 19(1-2):279, 1963.

Particles morphologically similar to Bittner virus particles were discovered in pellets obtained from high speed centrifugation of defatted and

decaseinated milk from Af/Dm and C57Bl mice, and from C3Hf/Hen spontaneous mammary tumors. On bioassay of (C57 x Af)F1 hybrids, the high speed pellet from Af/Dm undiluted milk caused tumors in 56% of mice, whereas the undiluted whey was tumorigenic in 36% and the centrifugal pellet at 10⁻¹ was tumorigenic in 0 and 30% (in 2 experiments). In a series of similar experiments using cell-free extracts from apparently spontaneous mammary tumors in C3Hf/Hen mice, highest tumor inducing properties were in a high speed pellet diluted 10⁻¹ (43%), although tumorigenicity was also present in some cell-free extracts (0-5% undiluted, 21% when diluted 10⁻²) and in centrifugal pellets (13% when undiluted).

63-903 A CONTRIBUTION TO THE STUDY OF ONCOGENIC VIRUSES. (E.) Violante, A. (Higher Inst. Health, Rome) and D. S. Bocciarelli. Acta Un. Int. Cancr. 19(1-2):424-427, 1963.

Systematic examination by electron microscopy of leukemic cells from rats bearing the transplantable Oberling myeloma failed to reveal any evidence for a viral agent. The observation is in agreement with the failure of others to transmit this tumor via cell-free filtrates. In the course of this study aspecific cell changes resembling virus particles were observed, and these were comparable to the changes observed in monkey kidney cells infected with the Echo 9 virus. The particles are believed to be due to alterations of cytoplasmic organelles, probably mitochondria.

63-904 REOVIRUS AND WOUND-TUMOR VIRUS: SEROLOGICAL CROSS REACTIVITY. (E.) Streissle, G. (Boyce Thompson Inst. Plant Res., Yonkers, N.Y.) and K. Maramorosch. Science 140(1):996-997, 1963.

Complement fixation took place up to and including a dilution of 1:128 for wound-tumor antiserum (from highly purified wound-tumor virus extracts of plant tumors), and of 1:64 for reovirus antigen (strains I, II or III grown on monkey kidney cells). Control tests (monkey kidney cells) were negative at 1:64 and 1:128, but not at 1:32. The sharing of a complement fixing antigen between a plant pathogen and a human pathogen is in agreement with previously reported morphologic and biochemical similarities between the 2 viruses.

63-905 IMMUNOLOGICALLY SPECIFIC ANTIGENS IN LEUKEMIC TISSUES. (E.) Greenspan, I. (U. Illinois Med. Sch., Chicago), E. R. Brown and S. O. Schwartz. Blood 21(6):717-728, 1963.

A positive reaction could be demonstrated by passive cutaneous anaphylaxis when the serum from an immunized subject (5-10% brain or lymph node filtrates of homogenates from leukemic (L) brains or Hodgkin's disease lymph nodes, or Freon

113 extracts; 0.1 ml intracutaneously and 0.9 ml i.m., repeated at 3 and 6 wk. followed by booster at 1 mo.) was inj. i.p. into guinea pigs, and the challenging antigen was obtained from either human or mouse L tissue. Positive results were also obtained when L tissue antigens were used to sensitize, and immunized human antisera were used to challenge. All other combinations of sera and antigens (normal brain or lymph nodes, normal mouse brain, sera from convalescents from viral diseases such as influenza, herpes simplex, hepatitis, or poliomyelitis) gave negative results. The specificity of the reaction was retained on adsorption with normal human or mouse brain, but was lost with L human or mouse brain. Extracted γ -globulin from positive sera gave a strong positive reaction. No false positive or false negative reactions were observed when sera from 9 volunteers inj. with L brain extract were reacted with L human brain, L mouse brain, or fluorocarbon extract of L brain, although the same sera had been negative prior to L inoc. The anti-L sera were negative with extracts of carcinoma tissues and with viruses such as herpes simplex, influenza, and poliomyelitis. Sera from 2 volunteers inj. with Hodgkin's disease node extracts reacted with Hodgkin's disease node extract and, to a lesser extent, with L tissue extracts, but not with other extracts. After 6 mo. of working with experimental leukemia, the sera of 6 workers (originally negative) gave positive reactions with L extracts, but at a lower titer than that found in the inj. volunteers. In contrast, sera from 24 normal adults and 6 children were negative to both L and normal brain extracts. Sera from 6 adults and 4 children with acute leukemia gave repeatedly negative results with all antigens. This finding remains unexplained. Organ specificity of the immune reaction was demonstrated by a strong positive and weak positive reaction to normal and L brain extracts, resp., observed in humans inj. with normal brain extracts. The reaction became negative on adsorption of the sera with normal brain tissues, and the non-adsorbed sera failed to react with Hodgkin's disease nodes. On immunodiffusion common precipitin bands were noted between normal and L tissue antibodies tested at high conc. However, in each case L antisera had at least 1 distinctly different band. The test was found to be highly specific and sensitive for the demonstration of antibodies in human and rabbit sera. Micro-precipitin tests also allowed rapid distinction of anti-L and anti-normal tissue sera. The human anti-L and anti-Hodgkin's disease node sera reacted positively with all human L antigens, but not against normal human tissue antigens. Fluorescein isothiocyanate conjugates with human anti-L sera (pooled from volunteers) reacted, when unadsorbed, with normal and L human brain impression smears. A greater degree of fluorescence was observed when conjugates were tested on L brain (+4 compared to +1-2). After adsorption with normal human liver or brain the conjugates reacted only with L tissues. The fluorescence appeared to be restricted to the cytoplasm,

adjacent to the nuclear membrane, and resembled inclusion bodies in pattern. When adsorbed γ -globulin was fractionated from anti-L sera, fluorescence was seen only with L brain impression smears. Although the highest degree of fluorescence was always observed with the homologous system, adsorbed human anti-L sera also reacted with L mouse brain impression smears, but not against normal mouse brain tissue impression smears. The specific antigenic differences observed between normal and L tissue extracts are thought to be due to the presence of a virus or of its alteration in L tissues.

63-906 OBSERVATIONS ON SERUM B₁₂ AND FOLATE ACTIVITY IN NORMAL AND LEUKEMIC RATS. (E.) Lynch, T. J. (Dept. Hematol., Hackensack Hosp., N.J.) and W. C. Moloney. Blood 21(6): 764-768, 1963.

Serum B₁₂ and serum folate activity in rats were similar to human levels, with a mean of $364 \pm 1 \mu\text{g/ml}$ for B₁₂, and of $129 \pm 27 \mu\text{g/ml}$ for the folate. Total body irradiation (450 r) or administration of 20-methylcholanthrene (20-ME; 180 mg total, details) did not alter either level significantly. However, Osborne-Mendel rats maintained on a vitamin A deficient diet had mean levels of B₁₂ and folate of $82 \mu\text{g/ml}$ and $78 \mu\text{g/ml}$, resp. Rats with induced myelogenous leukemia (5 from 450 r, 2 from 20-ME, 1 from 450 r plus 20-ME) had normal B₁₂ levels ($329 \mu\text{g/ml}$), and depressed folate levels ($86 \mu\text{g/ml}$), whereas rats with acute lymphatic leukemias (2 from 450 r) had increased B₁₂ levels ($1875 \mu\text{g/ml}$) due to hepatocellular necrosis and depressed folate levels ($62 \mu\text{g/ml}$). No significant abnormalities were noted in serum activities of rats with induced chloroleukemias (Shay).

63-907 SOME PROPERTIES OF THE FOWL VIRUS TUMOUR B 77. (E.) Thurzo, V. (Ul. C. Armady 17, Bratislava, Czech.), J. Smida, V. Smidova-Kovarova and D. Simkovic. Acta Un. Int. Cancr. 19(1-2):304-305, 1963.

A fibrosarcoma discovered in a White Leghorn hen and designated B 77 was transplantable to various birds including hens of various strains 1-12 months old, pigeons, turkeys, pheasants, and ducks. Takes were 100% in pigeons. The tumor was also transplanted successfully in 2/10 hamsters, all pretreated with tumor extract, cortisone, and hamster tumor s.c. according to the method of C. Oravec. On continuing subpassage in chicks latency had decreased from 6-9 to 4-6 days. A partially purified tumor preparation caused tumor at 5-9 days in 100% of ducks, when inj. i.m. (wing), whereas similar preparations of the Bryan's strain of Rous sarcoma were not successful. Intracerebral inj. of B 77 into 1-2-day-old chicks produced local tumors. In 1-day-old chicks i.v. virus caused hemorrhagic disease leading to death at 8-12 days, but no tumors in some animals, while others had liver, lung and heart tumors, but no

hemorrhagic disease. Inj. i.v. into older chicks failed to cause hemorrhagic disease. Of various partially purified preparations the fluorocarbon extract was most active with 0.004 μ g N/minimal infectious dose, compared to 0.015 and 0.052 for a preparation obtained by differential centrifugation, and a 5,000 \times g tumor extract, respectively. Gradient centrifugation, electron-microscopic, and filtration experiments indicate a particle size of 70-90 m μ . In cell culture, tumor cells released virus continuously into the supernatant over 21 days on collagen gels. The virus was completely inactivated at 39°C for 24 hr., produced tumor-neutralizing antibodies in adult hens and ducks, and was not affected by 1:1000 bovine serum, although the properdin reaction inhibits tumor growth.

908 URIDINE NUCLEOTIDE AND RIBONUCLEIC ACID METABOLISM IN THE MORRIS 5123 HEPATOMA. (E.) Reid, E. (Chester Beatty Res. Inst., Royal Cancer Hosp., London) and H. P. Morris. *Biochim. Biophys. Acta* 68(4):647-651, 1963.

Survey of metabolic alterations in uridine nucleotide and ribonucleic acid metabolism in dye-induced primary hepatomas and the 3-C slowly growing transplantable hepatoma originally induced by N-2-fluorenylphthalamic acid indicates that a rise in supernatant uridine acid RNase activity and a fall in soluble purine nucleotides is common to both hepatomas. On the other hand decreased levels of NAD in whole tissue or mitochondrial fractions, and increased activities of uridine phosphorylase and of the enzyme system converting aspartate to orotate are found in the azo hepatomas, but not in the 5123-C hepatomas. *In vivo* admin. of 6-C¹⁴-orotate (0.17 mg (10 μ C) 75 min. before sacrifice) to Buffalo strain bearing the 5123-C tumor (inoc. s.c. or i.m. 6 mo., experiment performed at 5 mo.) gave a consistently low recovery of radioactivity to about 10% that found in livers from non-tumor bearing controls. However, when the recovery of radioactivity in the RNA (mitochondrial, microsomal and supernatant) was related to the specific radioactivity of supposed precursors, the 5123-C hepatoma fractions showed a relative increase in labeling. The increase was highest in the supernatant fractions (5 \times if UDP and 3-5 \times if UTP assumed to be the precursor). There was also an increase in microsomal RNA to 36% of the control level. Results are considered in agreement with the hypothesis that in hepatomas there is a faster turnover.

909 OBSERVATIONS ON THE SURFACE OF CELLS INFECTED WITH ROUS SARCOMA VIRUS. (E.) P. K. (Dept. Path., U. Colorado Sch. Med., Denver) and N. Luykx. *Virology* 20(1):75-87, 1963.

Infection of virus-free chick embryo fibroblast cultures with about 1 FFU of Rous sarcoma virus

(RSV)/cell followed by fluorescent antibody staining showed viral antigen loosely attached to the cell sheet, decreasing in amount between 12-18 hr. 3-18 after infection. At 24 hr. newly formed viral antigen could be detected in the cells combined with granules first in long cytoplasmic protrusions (filopodia), later distributed uniformly over the cell surface. The granules increased in size and then coalesced to form patches of surface antigen. In sparsely seeded cultures almost all the cells were stained by RSV antibody by day 3 after infection. Electron microscopic study confirmed these results, with the first viral particles appearing on the second day after infection, mainly arranged in groups along the filopodia. After day 3 filopodia were infrequent, apparently due to breakage of those which remained attached to glass. Most of the infected cells had become rounded, appeared opaque and contracted, and were surrounded by a fibrous matrix containing many viral particles. Direct count of particles gave 50-300/cell on day 3, and a mean of 930 on day 4, and of 570 on day 5. These counts were in fair agreement with viral counts obtained by an indirect method. Concomitant electron microscopic and fluorescent antibody studies confirmed the identity of surface areas containing antigen and viral particles.

63-910 GROWTH AND PERSISTENCE OF FRIEND LEUKEMIA VIRUS IN TISSUE CULTURE. (E.) Moore, A. E. (Sloan-Kettering Inst. Cancer Res., New York). *J. Nat. Cancer Inst.* 30(5):885-895, 1963.

Numerous technics have failed to increase the yield of Friend leukemia virus in tissue culture. Mouse embryo tissue cultures exposed to leukemic cells from Friend virus-inoc. mice produced small quantities of virus for 633 days. Neither cytopathic effect nor growth of leukemic cells was observed. Mouse embryo cells exposed to leukemic filtrates and passed 30 times at weekly intervals produced leukemia when admin. to mice, but only erratically and unpredictably.

63-911 ISOLATION OF LEUKAEMIA VIRUS FROM THE TRANSPLANTABLE MAMMARY CARCINOMA OF C3HA MICE (RSM STRAIN) AND ITS ADSORPTION ON RED CELLS. (E.) Stepina, V. N. (Inst. Exp. Clin. Oncol., Moscow) and L. A. Zilber. *Acta Un. Int. Cancr.* 19(1-2):379-381, 1963.

When newborn C3HA and hybrid (C57 female \times C3HA male) mice were inoc. with 0.1 ml of rabbit or guinea pig RBC after their contact with a homogenate from a transplantable mammary carcinoma of spontaneous C3HA origin (RSM strain), generalized chloroleukemias developed in 27.5% of 84 after 22 mo.; the first case appeared after 9 mo. After inoc. of cell-free filtrates of the same tumor, 29.2% of 171 developed leukemia after an average latent period of 22 mo.; no mammary cancer was detected. Of 11 hybrid mice given 0.1 ml of a spontaneous C3HA mammary tumor filtrate, 4/11 developed mammary cancer after 8 mo.; no leukemia

was detected. Leukemia and mammary cancer did not develop in 66 mice given 0.1 ml of untreated RBC or in 89 untreated controls. Transplantation of cell-free filtrates of the chloroleukemias caused leukemias in 11/20 newborn mice, with a latency of 3.5-4.0 mo.

- 63-912 THE RELATIONSHIPS BETWEEN VIRUS AND CELL IN RAT SARCOMAS INDUCED BY ROUS VIRUS. (E.) Svoboda, J. (Inst. Exp. Biol. Genetics, Czech. Acad. Sci., Prague) and D. Simkovic. Acta Un. Int. Cancr. 19(1-2):302-303, 1963.

Rous sarcoma-induced sarcoma XC cells (passaged for 3 yr. in young rats) which induces malignant tumors in chickens which resembled Rous sarcomas and contained filterable virus similar to Rous virus in oncogenic and serological activity, was inoc. into chicks. Concentrations of 5×10^6 - 10^7 living XC cells produced lethal tumors in 3/6 and 6/6, resp.; lower conc. of living cells, thrice frozen and thawed XC cells (5×10^4 - 10^7) and supernatant fluid and conc. microsome fractions had no oncogenic activity. XC living cells passaged *in vitro* were oncogenic in chickens although culture medium and its sediment were not. The activity of cells cultivated *in vitro* was slightly higher than those passaged *in vivo* and activity did not decrease after cultivation with chick antiserum against Rous virus. Attempt to induce formation of free infective virus *in vivo* and *in vitro* with X-ray, UV or superinfection were unsuccessful. Analysis of cellular populations of tumor XC indicates that the capacity of XC cells to form the Rous virus is potentially present in the whole cell population.

- 63-913 DISTRIBUTION OF VIRUSES RECOVERED FROM TUMORS AS MEASURED BY HEMAGGLUTINATION INHIBITION TESTS. (E.) Moore, A. E. (Sloan-Kettering Inst. Cancer Res., New York). Acta Un. Int. Cancr. 19(1-2):273-275, 1963.

Screening of various species for anti-H virus antibodies using the hemagglutination-inhibition test showed anti-H-1, anti-H-3, or anti-both in 37/47 AxC (susceptible) rats, in 4/21 guinea pigs, in 1/15 bovines, and in none of 17 horses, 22 rabbits, 43 mice, or 12 dogs. In tests on 38 guinea pigs, antibodies were found only in 2 that had been kept in the laboratory for over 6 mo. Sera from 456 blood donors aged 1 to over 40 yr. were negative, including 20 sera each from India, South Africa, and Jamaica. Antibodies to the H-1, but not to the H-3 virus were found in 3/314 cancer pts. (2/3 had breast cancer); the sera of 8% more cancer pts. had a low level of activity which gave equivocal results in neutralization tests. Of 34 laboratory workers 1 showed anti-H-1 antibodies, and also neutralizing antibodies (= 5 log units of virus). No antibodies could be detected in 21 asymptomatic breast clinic pts., in 31 people taken ill in an

"epidemic" of sore throat, high fever, and prostration at the same time as the antibody-positive laboratory worker, or in 14 pts. attending an abortion and sterility clinic. Characteristics of the H viruses, and their sources are reviewed.

- 63-914 FATAL INFECTION OF AxC RATS WITH H VIRUSES. (E., Abstract) Moore, A. E. (Sloan-Kettering Inst. Cancer Res., New York). Proc. Am. Assn. Cancer Res. 4(1):45, 1963.

Five different isolates of the H-1 or H-3 viruses caused fatal disease in newborn AxC rats. The 2 H-1 virus strains used were highly virulent and of the three H-3 types, the RV strain was the least virulent. Of 315 rats surviving after 6-10 mo., 1 developed mammary adenoma at the age of 7 mo. Hemagglutination-inhibition tests on 51 AxC rats showed no antibodies against H-1, H-3 or RV viruses. It thus appears that the H-viruses are not highly oncogenic in AxC rats.

- 63-915 POLYOMA VIRUS: EXAMINATION BY GEL ELECTROPHORESIS AND DENSITY GRADIENT CENTRIFUGATION. (E., Abstract) O'Connor, T. E. (NCI, Bethesda), S. I. Oroszlan and P. T. Mora. Proc. Am. Assn. Cancer Res. 4(1):49, 1963.

A large plaque-forming strain of polyoma virus harvested from mouse embryo cultures was assayed for hemagglutinating activity (HA) and for infectivity (I) by starch-gel electrophoresis (at pH 8.6) and by density gradient centrifugation (utilizing synthetic macromolecular polyglucose). On starch gel electrophoresis HA migrated as a sharp band with I. However, in the density gradient, HA occurred in a well sedimenting sharp band (buoyant density 1.17 g/ml) and was also found near the solution surface. Only 5% of I was associated with these bands, whereas the remainder of I occurred at intermediate densities.

- 63-916 EFFECT OF HEMATOPOIETIC CHIMERISM ON THE COURSE OF RAUSCHER'S VIRAL MOUSE LEUKEMIA. (E., Abstract) Sinkovics, J. G. (Dep. Med., U. Texas M. D. Anderson Hosp., Houston) and C. C. Shullenberger. Proc. Am. Assn. Cancer Res. 4(1):62, 1963.

Mice (Balb/c) which are susceptible to Rauscher leukemia virus, were inj. at birth with spleen, bone marrow, thymus, and lymph node cells from adult C57Bl mice, which are relatively resistant to Rauscher leukemia. The Balb/c mice with hematopoietic chimerism had the same incidence of leukemia as controls, although viral multiplication was delayed, and incubation time of the leukemia was prolonged. Leukemias produced in the chimeras were predominantly of the host type e.g. erythroblastosis and stem cell leukemias.

- 63-917 ACTIVATION OF SERUM LACTIC DEHYDROGENASE BY A VIRUS FROM MICE TUMORS. (Ger.)

orgii, A. (Pathol. Inst., Ludwig-Maximilians-U., Munich, Germany), H. Bayerle, D. Brdiczka and H. Bl. Zschr. Krebsforsch. 65(4):334-341, 1963.

e CRA 1(2):#255, 1963.

-918 STUDIES ON THE MECHANISM OF SPONTANEOUS REGRESSION OF THE SHOPE RABBIT PAPILLOMA. (Abstract) Kreider, J. W. (Dept. Path., U. Pennsylvania, Philadelphia). Proc. Am. Assn. Cancer Res. 4(1):35, 1963.

Shope papilloma cells were obtained by infecting flaps of skin, washed free of antiviral antibodies, in short term organ cultures. Autografts of the resulting papillomas on rabbits in which papillomas had previously regressed either failed to develop or developed, and then regressed. The skin from regressor rabbits was shown to be fully capable of developing papillomas by grafting washed, virus treated fragments into the neck pouch of cortisone-treated hamsters. Results are considered consistent with the hypothesis that the rabbit can develop immunity to autologous papilloma cells.

-919 EVIDENCE FOR A MINUTE INFECTIOUS ENTITY. (E., Abstract) Riley, V. Sloan-Kettering Inst. Cancer Res., Rye, New York. Proc. Am. Assn. Cancer Res. 4(1):57, 1963.

Physicochemical studies were performed on a previously described infectious agent which causes elevation of lactic dehydrogenase and of other enzymes in mouse plasma. The agent passes through Selas 03 grade ceramic filters, filtration membranes with 10 mμ pores, and cellulose tubing. The integrity of the dialysis tubing was checked using the H-1 virus (diameter = 14-15 mμ). Measured diffusion measurement in a multilayered gel gave a diffusion coefficient greater than 10⁻⁶ sq. cm/sec, and a calculated equivalent spherical diameter of less than 0.2 mμ. Data on the size of the infectious particle indicate that it is smaller than known, infectious nucleic acid molecules.

920 RILEY'S ENZYMES ELEVATING VIRUS; A STUDY OF THE INFECTION IN MICE AND ITS RELATION TO VIRUS-INDUCED LEUKAEMIA. (E.) Mason, K. E. K. (London Hosp. Med. Coll., England), H. Adams and M. H. Salaman. Acta Un. Int. Cancr. 19(1-2):404-406, 1963.

The action of the Riley (R) enzyme elevating virus was investigated in non-tumor bearing mice. In 3 groups of mice were inj. with R only, leukemic cells only, or leukemic cells + R, the greatest elevation of plasma lactic acid dehydrogenase (LDH) was obtained with leukemic cells + virus; this effect was synergistic since it was much greater than the sum of the two components. In a study of the effect of R alone with another virus, Moloney (M; from

sarcoma 37) on latent period and leukemia incidence, inoc. mice were evaluated after 31 days. When R was inj. into newborn or 1-day-old mice + M at age 3-4 days, 23/42 mice developed leukemia and the 1st tumor appeared at 12 wk. When R + M were inoc. on days 3-4, values were 30/48 and 11; when M was inoc. on days 3-4 and R on days 6-7, values were 27/42 and 12; R + heated M on days 3-4 gave values of 3/37 and 21; after M + heated R, values were 31/45 and 12. Hence the Riley virus did not appear to shorten the incubation period or increase the incidence of leukemia due to the Moloney virus, despite the synergistic action of R on plasma LDH.

63-921 STUDIES ON AN AGENT ASSOCIATED WITH HIGH PLASMA LACTIC DEHYDROGENASE ACTIVITY. (E.) Yaffe, D. (Weizmann Inst. Sci., Rehovoth, Israel). Acta Un. Int. Cancr. 19(1-2):407-410, 1963.

The presence of a transmissible lactic dehydrogenase (LDH) augmenting agent (LA) was detected in the plasma of mice bearing Ehrlich ascites tumors, hepatoma 134, and sarcoma SBL₁ which had been transplanted over a long period of time; but not in spontaneous tumors, chemical carcinogen or irradiation-induced tumors, polyoma virus, AK virus or C57Bl agent-induced tumors. LA is believed to be a contaminant of transplants unrelated to the etiology of the malignancy. Moloney leukemic virus (MLV)-induced lymphomas contained LA believed to be derived from sarcoma 37 from which MLV originated. LA can grow and propagate *in vitro* by serial passages on primary mouse embryo tissue where it is not cytopathogenic. The agent disappeared upon trypsinization and replating (LA-negative sublines). A 3-5-fold increase in LDH within 48 hr. was observed after inj. of plasma from animals bearing this LA positive tumor or after transplants of it were made into mice. When animals were grafted with LA-negative tumors or "cured" sublines (by trypsinization), the LDH of the host plasma remained at a normal level for about 10 days, and increased sharply only after tumor growth was apparent. It is concluded that physiological changes related to tumor growth and the LA both can account for LDH elevation, the 2 mechanisms being unrelated. Starch gel electrophoresis revealed that inj. of mice with LA or grafts of LA-positive tumors augmented a whole series of normal LDH isozymes in the plasma of hosts. After the inj. of mice with an agent-free subline, the plasma did not differ from the normal during the first few days; later when tumor growth was apparent, a few additional fractions appeared. In the discussion V. Riley said virologists should employ the same rigid criteria for establishing lack of oncogenic properties as in judging potential inducing capabilities and to avoid use of the term "contaminant" to describe one member of a multi-virus complex in the absence of experimental evidence showing lack of a biological role.

63-922 EXPERIMENTAL STUDIES ON CARCINOGENESIS. (Jap.) Kurino, T. (Fukushima Pref. Med.

U., Japan), S. Sotozima, F. Tsuda, H. Sato, R. Fukuta, Y. Abe, K. Kuniwake, S. Matsuyama, T. Hashimoto and K. Takahashi. Nippon Naika Gakkai Zasshi (J. Jap. Soc. Intern. Med.) 51(4):428-429, 1962.

In AKR or C58 mice with spontaneous leukemia, the diploid number of chromosomes of leukemic cells in 5 strains was 40, in 2 strains 41 and all were rod-shaped; the normal number in the mouse is 40. Chromosome number in cells of breast tumor of C3H, C58 and dd strains was 39, 40, 41 or 42 and again were rod-shaped. The fact that there was no marked difference in chromosome numbers or shape in these 2 types of cancer cells suggests their origin from normal body cells. In both types of cancer cells examined by the electron microscope, inclusion bodies were observed in the intercellular space in cells of leukemic mice and on the cell wall or in the intercellular space, vacuoles or mammary ducts in breast cancer cells. Cell-free organ extract from AKR leukemic mice when inj. into normal mice led to the development of leukemia after 1.5-6 mo.; chromosome number was 39 or 41 and were V- and dot-shaped. After serial transplantation of leukemic or breast tumor cells into the same strains of mice, there was usually no change in number or shape of chromosomes except for the appearance of an abnormal dot-shaped chromosome in one strain of AKR mice after 18 passages of leukemic cells. An abnormal V-shaped chromosome appeared in the 2nd passage of the 1 strain, and 2 target chromosomes were observed in the 20th generation in C58 mice. In succeeding passages, there were no further changes in number or shape of chromosomes even though the hosts developed leukemia in each case. Upon electron microscopy of transplanted leukemia cells, no virus or inclusions bodies were found. The authors conclude that the virus has an influence on spontaneous leukemia or breast cancer but after transplantation, growth of cancer cells was autonomous.

63-923 A FLUORESCENT ANTIBODY STUDY ON THE FORMATION OF SIMIAN VIRUS 40 IN MONKEY KIDNEY CELLS. (E.) Diderholm, H. (U. Uppsala, Sweden). Acta Path. Microbiol. Scand. 57(3): 348-352, 1963.

When the fluorescent antibody technic was used to study the formation of simian virus 40 (105.5 TCID₅₀ of a strain neutralized by anti-serum to strain 776), in cell cultures of African green monkey kidney cells, a few nuclei contained specific fluorescent material 2 days after infection when nuclear swelling was observable; in 5 days 50% of the nuclei were affected. A specific cytoplasmic fluorescence appeared in 8 days which increased in time as nuclear fluorescence decreased or disappeared. Cytopathic changes were also observed beginning on day 5 after infection.

63-924 BIOLOGICAL CHARACTERS OF POLYOMA VIRUS AND THEIR RELATION TO TRANSPLANT IMMUNITY. (E., Abstract) Hare, J. D. (U. Rochester, N.Y.) and H.R. Morgan. Proc. Am. Ass. Cancer Res. 4(1):26, 1963.

Three polyoma virus (PV) strains, SE3049, SE210 and PV1P were examined for relationships between oncogenicity and ability to produce transplantation immunity against PV-induced hamster tumors. The SE3049 and PV1P strains were identical serologically, produced large plaques, high titer of hemagglutinin, and sarcomas in 100% of newborn hamsters. After many passages in L cells the SE210 strain was serologically distinguishable from the other two, produced little hemagglutinin, small plaques, and sarcomas in less than 30-50% of newborn hamsters. The 2 SE strains produced immunity against hamster tumor cell lines induced by either of the 2 strains, but the PV1P virus was unable to protect against either cell line. The data suggest that the capacity to produce transplantation immunity is not related directly to oncogenicity, and that the two are separable phenomena. A study of replication of SE210 virus in L cells has shown that at times a majority of the cells carry virus in their cytoplasm and can complete mitosis. (See also CRA 1(1):#103, 1963.)

63-925 STUDIES ON INDUCED RESISTANCE AGAINST ISOTRANSPLANTS OF VIRUS-INDUCED LEUKEMIA. (E., Abstract) Glynn, J. P. (NCI, Bethesda). Proc. Am. Assn. Cancer Res. 4(1): 23, 1963.

Consistent but weak resistance to transplantable Moloney virus-induced leukemia was observed in isologous BALB/c and F₁ (BALB/c x DBA/2) hybrid mice pretreated with X-ray inactivated tumor tissue. Tumors also grew more rapidly and fewer cells were required to elicit tumor growth in X-irradiated than in normal mice. Since the neoplasms contained low conc. of the tumor virus (approx. 4-5 logs less than standard virus preparations), the influence of the virus on induced resistance was investigated. In weanling BALB/c mice infected with a relatively low conc. of the virus and inoc. with isologous tumor at wk. intervals, resistance to isotransplants was demonstrable 3 wk. after virus inoc. No resistance was observed in infected mice challenged at 9, 12 and 15 wk. after virus inoc. Disappearance of induced virus resistance in the virus infected animals appears to be consistent with the observation that virus infected BALB/c mice invariably succumb with primary Moloney virus-induced leukemia.

63-926 MULTIPLICITY OF CELL RESPONSE TO THE BAI STRAIN A (MYELOBLASTOSIS) AVIAN TUMOR VIRUS. VI. ULTRASTRUCTURAL ASPECTS OF ADENOSINETRIPHOSPHATASE ACTIVITY OF NEPHROBLAST CELLS AND VIRUS. (E.) De Thé, G. (Duke U. Med. Ctr., Durham, N.C.), H. Ishiguro, U. Heine, D. Beard and J. W. Beard. J. Nat. Cancer Inst. 30(6):1267-1301, 1963.

dney tumors with characteristics of nephroblastomas were induced by inoc. of BAI strain A virus to white Leghorn chickens, line 15. Ultracytochemical studies of tumors revealed adenosinetriphosphatase (ATPase) only at the brush borders of cells corresponding to analogous elements of the proximal convoluted tubules and at the membrane of cells resembling those of the distal convoluted tubule of the normal nephron. Virus budded from the membranes of the latter cells reacted positively for ATPase. Rous sarcoma and cartilage cell membranes and those of proximal and convoluted tubules were negative for ATPase as were the virus-like particles associated with these membranes. Virus in plasma fillets of chickens with myeloblastosis gave a pronounced positive ATPase reaction. These findings support the view that viral ATPase in the nephroblastoma arises directly from incorporation of the enzyme into viral particles as they are budded from the membrane.

927 COMPARATIVE ULTRACYTOCHEMICAL STUDY OF ENZYMIC (ADENOSINETRIPHOSPHATASE) HOMOGENEITY OF AVIAN TUMOR VIRUSES. (E., Abstract) Thé, G. (Duke U. Med. Ctr., Durham, N.C.), Beard and J. W. Beard. Proc. Am. Assn. Cancer Res. 4(1):16, 1963.

Ultracytochemical studies of the thymus of birds with BAI strain A virus-induced myeloblastosis revealed ATPase activity of the virus (marked at the periphery of individual virus particles with lead phosphate). The enzyme activity was related to the activity of the cell membrane. Similar work with tissues of the BAI strain A virus-induced nephroblastoma showed that when budded from cell membranes with enzyme, the virus was active, but from cell membranes without ATPase was inactive. (See preceding abstract.) Virus from blood plasma of birds with myeloblastosis was highly homogeneous with respect to enzyme activity. Marked differences have been observed on preliminary surveys of other viral strains.

928 EFFECT OF INJECTED FROG-KIDNEY TUMOR EXTRACTS ON DEVELOPMENT OF TUMORS UNDER PROMOTING CONDITIONS. (E.) Rafferty, K. A., et al. (Dept. Anat., Johns Hopkins U. Sch. Med., Baltimore, Md.). J. Nat. Cancer Inst. 30(6):1003-1113, 1963.

The laboratory incidence of Lucké tumors in 69 *Rana pipiens* from the northern Lake Champlain area kept at 23-30°C with adequate feeding was 4.4% after 11 mo.; that for 67 frogs inoc. with tumor extracts homogenized by 2 different methods (0.25-1.0 ml i.p., i.v. or by dorsal lymph sac) was 25.5%. The rate of tumor formation in inoc. frogs was accelerated for several months before both groups eventually reached the same incidence. After 2-4 mo., tumor incidence was 10% for 168 inoc. frogs and 7% for 72 controls; after 5-11 mo., 25.2% for 111 inoc. frogs and 0.8% for 115 controls. Frogs arriving at the laboratory had a tumor incidence of 4.6%, close

to the 2.7% figure reported by Lucke. The data support the hypothesis that the tumors are virus-induced and that transmission is facilitated under crowded laboratory conditions.

63-929 CHROMOSOME ANALYSIS OF THREE VIRUS-ASSOCIATED CHICKEN TUMORS: ROUS SARCOMA, ERYTHROLEUKEMIA, AND RPL12 LYMPHOID TUMOR. (E.) Pontén, J. (Wistar Inst., Philadelphia). J. Nat. Cancer Inst. 30(5):897-921, 1963.

Qualitative and quantitative chromosome studies of 34 metaphases from 6 sources of normal primary embryonic cells grown in tissue culture and cells aspirated from femoral bone marrow of 2-4-week-old chickens revealed a mode of 78; a similar mode was obtained from analysis of 39 metaphases from 6 sources of erythroleukemia cells and 55 metaphases from 11 sources of Rous sarcoma cells (RS) although 1 chicken had chromosome numbers of 80 or higher. Analysis of 39 metaphases from 7 sources of homotransplantable RPL12 lymphoid tumor cells disclosed hyperdiploidy with counts from 80-84. Qualitative analysis of the morphologically distinctive chromosomes showed no abnormality; hyperdiploidy was probably due to an increase in the number of microchromosomes smaller than #13. Triploidy was found in the normal as well as all 3 tumor cell populations. A high proportion of cells in mitosis was found among RPL12 lymphoid tumor and erythroleukemia cells; a moderate proportion among normal cells and the aberrant RS; and a low proportion among the remainder of RS cells.

63-930 CYTOGENETIC STUDIES OF HAMSTER KIDNEY CELL CULTURES TRANSFORMED BY THE SIMIAN VACUOLATING VIRUS (SV40). (E.) Cooper, H. L. (Nat. Inst. Dental Res., Bethesda) and P. H. Black. J. Nat. Cancer Inst. 30(5):1015-1025, 1963.

Cytogenetic studies were performed on transformed cell cultures arising in monolayers from trypsinized renal cells of golden Syrian hamsters exposed to 106.5 TCID₅₀ SV40 virus for 24 hr. Colonies of rapidly growing transformed cells emerged after a latent period of 3-6 wk. revealing chromosomal aberrations such as breakage, translocation and deletion, with chromosome numbers in the diploid range although abnormal polyploids were also present. On serial passage these cells were rapidly overgrown by those with chromosome numbers in the triploid and tetraploid range. A tendency for metaphase chromosomes to group into clusters was found. Karyotype analysis disclosed irregular replication of different groups of chromosomes without presence of a unique stemline. It is concluded that SV40 produces a biochemical growth stimulus on which are superimposed processes producing aneuploidy.

63-931 EFFECT OF EXTRACT FROM HUMAN CONDYLOMA ACUMINATA ON CULTURES OF VAGINAL

EPITHELIUM. (E.) Chistova, M. M. (Lab. Path. Morph. Inst. Oncol., Leningrad, USSR). *Acta Un. Int. Cancr.* 19(1-2):422-423, 1963.

Cultures of human vaginal epithelium grown with a saline extract from human condylomas acuminata displayed considerably increased capacity to proliferate as early as 6-7 days after extract addition compared with normal controls, controls with added human vaginal mucosa extract or inactivated condyloma acuminata extract. Experimental cultures showed evidence of fibrinolytic activity, bi-, tri-, and polynuclear cells due to amitotic nuclear division, enhanced mitotic activity, polymorphism, appearance of giant cells, and impaired ribonucleoprotein synthesis indicated by an increased cytoplasmic basophilia, basophilic granules, vacuolization of the nucleus and increased nucleolar size. Similar changes were found in cultures grown with Shope papilloma extracts. Negative results obtained on biological control tests in rabbits appear to be due to the species specificity of the agent.

63-932 RELATIONS BETWEEN THE PATHOGENIC AND ANTIGENIC EFFECT OF THE VIRUS OF MYELOID LEUKAEMIA. (E.) Bielka, H. (Exp. Cancer Res., Ger. Acad. Sci., Berlin, Berlin-Buch), Yü Yen Chang and F. Hoffmann. *Acta Un. Int. Cancr.* 19(1-2):390-392, 1963.

In mice the induction of leukemia by the virus of myeloid leukemia after treatment with heat to 56°C was 0% of 41 animals; treatment with trypsin, 17.3% of 58; ether, 5.8% of 104; saponin, 7% of 72; deoxycholic acid, 1.6% of 123; formalin, 1.7% of 58 as compared with no treatment, 72% of 896; the spontaneous leukemic rate was 0.6% of 1027. The induction of leukemia by this virus after treatment with normal rabbit serum was 61% of 74; antiserum (A-S) against untreated filtrate, 6.4% of 47; A-S against heated filtrate, 37.5% of 32; A-S against trypsin-treated filtrate, 43% of 44; A-S against ether-treated filtrate, 73% of 22; A-S against deoxycholic acid-treated filtrate, 64% of 25; A-S against formalin-treated filtrate, 2.3% of 43. Heating as well as treatment of virus with trypsin, ether, saponin and deoxycholic acid inactivated or significantly reduced both the leukemogenic and antigenic effect to the same degree; formalin completely inactivated the leukemogenic effect while the antigenic effect was maintained. It is concluded that the virus-RNA constitutes the leukemogenic component and the virus-lipoprotein constitutes the antigenic component; together they are responsible for the full activity of the infectious nucleic acid.

63-933 TRANSMISSION OF FILTERABLE AGENTS FROM RAT CHLOROLEUKAEMIA INDUCED BY CELL-FREE EXTRACT FROM A RAT TUMOUR. (E.) Svec, F. (Oncol. Res. Inst., Bratislava, CSSR) and E. Hlavay. *Acta Un. Int. Cancr.* 19(1-2):374-376, 1963.

The cell-free supernatant of rat chloroleukemic organs (0.2 ml s.c. or i.v.) in rat embryos 3-4 days prior to birth or into weanling Wistar rats produced leukemia in 3% of 201 with an av. survival time (AST) of 545 days; after 0.02 ml (intracerebrally (i.c.); or intra-embryonally (i.e.)), results were 2.5% of 157, AST was 271 days. In the same groups 29.3% and 47.7%, resp., developed cirrhosis + hepatitis with AST of 518 and 290 days, resp.; tumor incidence was 8.5% and 0.6%, resp. No leukemia or other malignancies were found in rats inj. with high speed sediment (80,000 x g for 1 hr.); gradacol membrane filtrate (porosity to 275 mμ) or high speed sediment inactivated at 75°C. Incidence of hepatitis + cirrhosis in these 3 groups was 79.3% of 150; 82.3% of 43; and 2.5% of 80, resp., with AST of 160; 112; and 145 days, resp. The high speed sediment from cirrhotic rat liver (0.02 ml i.c. or i.e.) produced only leukemia in 2% of 85 with an AST of 232 days. The incidence of hepatitis + cirrhosis was 67% with an AST of 126 days. Inj. of cirrhotic plasma (0.02 ml i.c.), chloroleukemic plasma (0.02 ml i.c.), high speed cirrhotic liver sediment (0.02 ml i.c. inactivated at 75°C) and high speed sediment of normal liver and brain (0.02 ml i.c.) did not produce leukemia or any other malignancy. Incidence of hepatitis + cirrhosis for the 4 groups was 93% of 16; 10% of 20; 5.5% of 108; and 0% of 100, resp., with AST of 116; 86; 206; and 210+ days (at time of report, resp.

63-934 THE TRANSMISSION OF THE VIRUS OF MYELOID LEUKAEMIA OF MICE BY THE MILK. (E.) Krischke, W. (Inst. Exp. Cancer Res. German Acad. Sci., Berlin-Buch) and A. Graffi. *Acta Un. Int. Cancr.* 19(1-2):360-361, 1963.

The incidence of leukemia among untreated filial generations of Agnes-Bluhm mice (A-B; spontaneous leukemia incidence less than 2%) descended from parents treated with myeloid leukemia virus filtrates from birth was for the F₁ generation, 22% of 433 mice with a mean latent period (MLP; days) of 372; for F₂, 9% of 970, with MLP of 437; for F₃, 10% of 638, MLP of 451; and for F₄, 4% of 377, MLP of 462. For F₁ mothers, inoc. with virus incidence was 35% of 78, MLP, 240. The spontaneous leukemia rate was less than 1% with MLP of 365. The leukemia rate among F₁ progeny of A-B and CB₁ virus-infected mothers, suckled by normal mothers was 4/107, approx. 4% (of which 1 was a chloroleukemia) MLP was 142; of 40 litters, 5% showed leukemia in 1 or more mice. The leukemia rate among 56 F₁ progeny of normal mothers, suckled by virus-infected mothers was 54% of 56, (7 were chloroleukemias) with MLP of 145. Of 19 litters, 74% showed leukemia in 1 or more mice. It is concluded that vertical transmission of the virus of murine myeloid leukemia is mainly affected by mother's milk and to a much lesser degree by intrauterine factors.

63-935 THE LEUKAEMOGENIC EFFECT OF CELL-FREE FILTRATES FROM TWO TRANSPLANTABLE RAT

COSES. (E.) Gimmy, J. (Inst. Exp. Cancer
., Ger. Acad. Sci., Berlin-Buch) and A.
ffi. Acta Un. Int. Cancr. 19(1-2):385-389,
1963.

Cell-free filtrates from graft generation (GG)
of transplantable rat leukemia R204, a myeloid
form (originally from a cell-free filtrate of a
mouse leukemia) admin. to newborn Wistar rats
(3-0.5 ml s.c.) and Agnes-Bluhm mice (0.1-0.2
ml s.c.) produced leukemias in 29% of 31 rats
and 75% of 16 mice, resp. Passages 2-15 were non-
tumorigenic in rats, although in mice leukemia
developed in GG 2 (17/20), GG 9 (21/29), GG 11
(1/22) and GG 12 (25/40) but not in GG 15 (0/14).
In type, myeloid leukemia predominated (mouse
51/86; rat 44% (4/9)). Similar admin. of
cell-free filtrates from GG 2 of rat leukemia
R9, a lymphatic form (also originally from
mouse leukemia), produced leukemia in 71% of 31
mice after 161 days (20 lymphoid and 2 mixed
lymphoid and myeloid); after further transplanta-
tion the only leukemia was in GG 9 (1/6). In
mice, GG 6, 9 and 18 produced leukemia in 38% of
10, 88% of 9; and approx. 30% of 10, resp. Of
leukemias produced, 52% were myeloid; approx.
20% were lymphoid; 20% were reticulum cell;
28% were nonclassifiable. A cell-free filtrate
from the induced lymphoid leukemia produced by
GG 2 of R469 in rats produced leukemia in approx.
100% of 8 mice, (3 myeloid, 1 reticulum cell). It
was concluded that mice react to the virus by de-
velopment of the myeloid form even when the virus
was obtained from lymphoid leukemias. In rats the
histological type probably depended on the origin
of the filtrate. It is believed that rats do not
react to later transplantations because the virus
content of the filtrates decreases to a level
below the threshold dose for rats.

936 STUDIES ON VIRUS-INDUCED RETICULAR
NEOPLASMS IN BALB/c MICE. (E.)
Hensley, P. G. (Detroit Inst. Cancer Res.) and
D. Soule. Acta Un. Int. Cancr. 19(1-2):356-359,
1963.

In BALB/c mice were inoc. at 0-7 days of age
with cell-free extracts containing the agent of
reticulum cell sarcoma (RCS), 68/150 developed
in 2-9 mo.; 10/150 lymphosarcoma (L) after
mean latent period of 237 days, 9/150 RCS + L
(2 days), 36/150 hyperplasia (180 days),
compared with 183 controls, 2 of which developed
none RCS in 9 mo. RCS and L could be dis-
tinguished histologically and by the fact that
transplantability of RCS was low while that of
L was high. One extract induced only RCS in
19 while in another which induced neoplasms
10/16, RCS was seen in 3, L in 7. Cell-free
extracts induced disease in 6/6 MABA mice but
none in 11 DBA/2 or 13 C3Hf mice. When mice
were inoc. at 0, 2, 5, 7, 14, and 28 days of
age, disease developed in 0/4; 6/8; 2/5; 2/6;
and 0/3, resp., after mean latent periods of
1348 days. Of the mice inj. at 2 days of age,
developed RCS, 1 L and 1 RCS + L; of those inj.
at 5 and 7 days of age, 1 of each group developed

RCS or L. Extracts from hyperplastic tissue which
had not progressed to malignancy were capable of
inducing RCS in about 70% of mice of different ages.
Since mice sacrificed from 38-252 days after inoc.
showed evidence of hyperplasia, while those sacri-
ficed from 229-305 days showed neoplasia, it may
be that the neoplastic agent does not induce a
direct transformation of normal to neoplastic
cells. In tissue cultures, the neoplastic agent
induced neoplasms in 3/10 (1 RCS, 2 RCS + L);
6/9 (1 RCS + L, 5 L); 5/60; and 2/9 (1 RCS, 1 L)
after 21, 39, 12, and 312 days, resp.

63-937 POLYOMA VIRUS AND MOUSE KIDNEY
ORGANOGENESIS IN VITRO. (E.) Vainio,
T. (Dept. Physiol. Zool., U. Helsinki, Finland),
L. Saxen, S. Toivonen and J. Rapola. Acta Un.
Int. Cancr. 19(1-2):306-308, 1963.

Histochemical studies of isolated ureteric buds,
metanephrogenic mesenchyme, and salivary
epithelial and mesenchymal rudiments from 11-day-
old mouse fetuses infected in vitro with polyoma
virus (PV) revealed that only ureteric buds were
resistant to infection. During cultivation of
metanephrogenic mesenchyme in vitro, branching
of ureteric buds and development of distal
portions of tubules were observed with spinal
cord tissue as the inducer. Infection at various
stages with PV showed a genuine resistance of
kidney tubules regardless of their origin. It is
suggested that the in vivo resistance breaks down
near term as the result of a steroid hormone
imbalance. The importance of the interaction
of ureteric bud and metanephrogenic mesenchyme
for viral susceptibility is stressed.

63-938 LONG-TERM MICROKINEMATOGRAPHIC STUDIES
OF ACTION OF POLYOMA VIRUS ON ORGAN
CULTURES OF MOUSE SALIVARY GLAND RUDIMENTS. (E.)
Morgan, W. D. (NCI, Bethesda) and C. J. Dawe.
Acta Un. Int. Cancr. 19(1-2):309-317, 1963.

Time lapse cinematographic studies of excised
submaxillary gland rudiments of C₃H/BiLW mouse
embryos infected by polyoma virus (PV), from a
pool which induced salivary gland tumors in vivo
in more than 75% of inoc. newborn mice in less
than 6 mo., revealed that on days 9-10, vacuoles
appeared in the cytoplasm of peripheral mesenchyme
cells; cells died and necrosis progressed centrally,
so that by day 14, most of the connective tissue
cells appeared dead. At variable intervals after
25 days, morphological alterations were observed
in the epithelial cells: cells were larger and
had larger nuclei and nucleoli; some were necrotic
and some were undergoing mitosis. Reshaped ducts
and buds were composed of these altered cells.
There was no overall increase in cell mass. Late
changes in control cultures indicated that with
increased time, uninfected rudiments might show
changes similar to those occurring earlier in
infected rudiments. Histologically, epithelium
of infected cultures had undergone transformation
characteristic of the response to PV while controls
had not.

63-939 ON RELATIONSHIP OF POLYOMA VIRUS AND
TISSUE CULTURE OF MONKEYS. (E.)

Adjigitov, F. I. (Inst. Exp. Path. Acad. Med. Sci., Soukhoumi, USSR). Acta Un. Int. Cancr. 19(1-2):332-333, 1963.

Kidney cell cultures of adult Macacca mulata were resistant to polyoma virus even when cultures were X-irradiated to reduce resistance. When cultures of embryo kidney cells were infected with polyoma virus (hemagglutinin titer (HA) 1:256/ml) viral multiplication occurred after 2-5 wk. in fibroblast cultures (from 1.5- and 3-month-old minced embryos) and in epithelial cultures (from 3-month-old embryo kidneys) but no cytopathogenic effect of malignant transformation occurred. During passage in mouse embryo tissue culture a viral titer of 10^{-4} - 10^{-5} /ml was demonstrated in the 1.5- and 3-month-old embryo cultures with restoration of HA and cytopathogenic effects. No such activity was recorded in fibroblast or epithelial cells from 5 mo. old embryos. Hamsters inoc. with infected cultures from 1.5-3-month-old embryos developed tumors within 35 days. No such activity was found in cells from 5-month-old embryos or in adult kidney cells. The infectious process in monkey cell cultures had the appearance of a latent virus infection. Hemagglutination inhibition tests in fluids of normal tissue cultures demonstrated the presence of nonspecific, heat stable inhibitors of viral hemagglutination.

63-940 FURTHER STUDY OF HAEMOCYTOBLASTOSIS-
RETICULOSIS VIRUS OF MICE. (E.)

Mazurenko, N. P. (18 Petchatnikov, Moscow). Acta Un. Int. Cancr. 19(1-2):341-343, 1963.

When filtrates of organs containing hemocyto-blastosis-reticulosis virus (H-RV) from a number of mice were inoc. (0.1-0.2 ml s.c.) into 37 white rats 1-3 days of age, 30% developed leukemia after a mean latent period (MLP) of 7.4 mo. in passage 0; no controls given heat-inactivated virus developed leukemia. Cell-free filtrates of spleen, lymph nodes and tumors of leukemic rats produced leukemia in 73% of 71 inoc. newborn rats after a MLP of 5.6 mo. in passage 1. Material passaged 2 x in rats produced leukemia in 66% of 21 mice after a MLP of 5.8 mo. Large thymic tumors were found more often in rats, while peripheral lymph node enlargement was seen more often in mice. The frequency of thymic tumors was 95%; splenomegaly, 66%; enlargement of liver, 57%; of peripheral lymph nodes, 43%; and tumors of mesenteric lymph nodes, 19%. All induced leukemias in both mice and rats were of the hemocyto-blastosis-reticulosis type. Antibodies against the leukemia antigen were detected in the sera of 5/7 infected mice; titers

were 1/120-1/320. The antibodies were detected in the sera of 3/7 H-RV-infected mice in which symptoms were absent; the titers were 1/20-1/80. The complement fixation reaction with normal mouse tissue antigens was negative in all cases.

63-941 STUDIES ON A VIRUS ISOLATED FROM A
CALF AFFECTED BY LYMPHATIC LEUKEMIA.

1. COMPARISON OF THE VIRULENCE OF THE VIRUS CULTIVATED ON CHICK EMBRYO AND ON TISSUE CULTURE. (E.) Papparella, V. (Inst. Infect. Dis., Naples). A. Cali and G. B. Rossi. Acta Un. Int. Cancr. 19(1-2):336-340, 1963.

When 7-day-old chick embryos were inj. by the yolk sac route with a virus, originally isolated from the lymph nodes of a 45-day-old calf dead of acute lymphatic leukemia, passaged 66 x in the yolk sac of 7-day-old embryos (L66) or 16 x in calf kidney cell tissue culture (TC16), the pathogenic activity of TC16 remained steady at a high level on serial dilutions while that of L66 diminished rapidly. The mortality rate among embryos given undiluted TC16 fluid, a 1:2 dilution 1:4, 1:8, 1:16 was 66% of 30; 61% of 29; 57% of 28; 44% of 30; and 37% of 30, resp. That for embryos given undiluted L66 fluid and the same dilutions was 54% of 29; 44% of 30; 30% of 27; 24% of 30; and 17% of 29, resp. For controls inj. with heat inactivated TC16 culture fluid 0%; 4%; 0%; 3.3%; and 0%, resp. Data from embryos dead from TC16-induced leukemias showed greater variability with only 33/78 animals dead on day 3 and 7/78 animals still alive on day 8, while 36/48 embryos dying from L66 were dead on day 3, and only 1/48 was still alive on day 8. The TC16 LD₅₀ was 0.170; that of L66, 0.893; P value was 0.045. No significant histological differences were found in embryos receiving TC16 and L66.

63-942 CHROMOSOME STUDIES ON SERIALY TRANS-
PLANTED ROUS SARCOMA IN THE RAT. (E.,
Abstract) Nichols, W. W. (South Jersey Med. Res. Found., Camden, N.J.), A. Levan and C. G. Ahlström. Proc. Am. Assn. Cancer Res. 4(1):48, 1963.

A sequence of chromosomal changes was observed on viral induction and on serial transplantation of Rous sarcoma virus (Schmidt Rupp Strain) through approx. 50 tumor generations in rats. In the initial tumor induction and early tumor passages, the stemline chromosomes were either diploid or near-diploid. After several passages there were frequent changes in chromosome structure which, in late passages became permanent and were accompanied by changes in ploidy. Evidence is in agreement with a somatic mutation theory of carcinogenesis at the level of point mutation and/or chromosomal breakage.

63-943 STUDIES PERTAINING TO THE ABILITY OF THE VIRUS OF MOUSE MYELOID LEUKEMIA TO GROW IN TISSUE CULTURE. (Ger.) Graffi, A. (Inst. Exptl. Cancer Res., German Acad. Sci. Berlin, Berlin-Buch), L. Baumbach, T. Schramm and J. Bierwolf. *Zschr. Krebsforsch.* 65(4):385-395, 1963.

Inoculation of mice (Agnes Bluhm strain) with culture fluid from Maitland or roller tube cultures infected with cell-free filtrates (g-4) of mouse SOV 16 leukemia did not increase the incidence of leukemia (11/545) compared to culture fluid alone (2/104). When trypsin was added to the mouse embryonic tissue, the leukemia virus formation continued for several wk.; inoc. into newborn mice of the cell-free nutrient medium from cultures of different ages resulted in the development of leukemia in 1/4 (4-day old culture); 3/3 (7-day culture); 1/3 (11-day culture); and 1/4 (21-day culture, with one questionable leukemia). The hematologic form of the leukemia varied, some were chloroleukemias. The medium of roller tube cultures made from lymph node tissue of a mouse infected with viral myeloid leukemia was changed every 2-3 days. Cell-free filtrates made from 4-5-day-old cultures induced leukemia in 56.5% of inoc. mice; after 6-10 days, 58.5%; after 38-44 days, 29%. Incubation of g-4 filtrate at 37°C for 24 or 48 hr. and inoc. into mice resulted in 0/21 cases of leukemia compared to 6/12 cases with fresh filtrate. The cell-free medium from a 20-day-old culture caused 4/25 cases of leukemia when fresh, and 0/25 cases after 24 or 48 hr. The admin. of cell-free leukemia filtrates to newborn mice induced leukemia (2 experiments) in 33/44 and 31/45. Electron microscopic study showed that the virus particles reproduced chiefly on the outer membranes of the leukemic cells by means of budding and constriction.

63-944 MYXOVIRUS-LIKE STRUCTURE OF AVIAN MYELOBLASTOSIS VIRUS. (E.) Eckert, A. (Max-Planck-Inst. Virus Res., Tübingen, Germany), R. Rott and W. Schäfer. *Zschr. Naturforsch.* (B) 18(4):339-340, 1963.

Electron microscopic study of ultracentrifugates from frozen plasma of chickens with leukemia due to the myeloblastomatosis virus (MB) showed little structural detail unless the virus was disrupted by brief exposure to Tween 80. On negative staining of the virus preparations the particles revealed small surface spikes, resembling in shape and size those described for myxoviruses. The internal viral component in partially disrupted particles was a filament 4 mμ in diameter, and of undetermined length, ranged in the form of an intricate coil. The filaments differ slightly from the broader and more rigid internal structures of the NDV-mumps-rainfluenza viruses, which also have a central

63-945 TUMORIGENICITY OF SIMIAN PAPOVAVIRUS SV40 AND OF VIRUS-TRANSFORMED CELLS.

(E.) Ashkenazi, A. (Dept. Virol., Baylor U. Coll. Med., Houston, Texas) and J. L. Melnick. *J. Nat. Cancer Inst.* 30(6):1227-1265, 1963.

When random bred hamsters received simian papovavirus (SV40, 106.2 TCID₅₀ s.c.) within 12 hr. of birth, 22/28 developed tumors at the site of inoc. after a latent period of 4-8 mo. Of 12 tumors tested, 8 yielded virus (titer range 10^{3.5}-10^{5.8} TCID₅₀/g of tumor); of 9 tested, 4 developed antibodies (titer range 1:4-1:16); when given 0.2 ml SV40 s.c. all responded in 2 wk. with titers of 1:256. Fluorescent antibody studies revealed antibodies to be concentrated in the nucleus. When 2 primary tumors which failed to yield SV40 were transplanted into hamsters, 70/76 developed tumors; 0/10 tested had detectable SV40; 0/20 had antibodies 2-3 mo. after tumor appearance. No virus was recovered when tumor cells were assayed 8 x during 20 tissue culture passages. Trypsinized fetal lung fibroblasts infected in the 10th passage with SV40 viral multiplicities of 1 (X1) and 10 (X10) were morphologically transformed at the 22nd passage and the 21st, resp., after 130 days, to epitheloid cells in which virus yield was reduced. Transformed cells failed to produce tumors when 2 x 10⁵ cells were inoc. into the hamster cheek pouch. Similarly SV40-infected trypsinized hamster embryo cells (lines X1 and X10), were transformed; no virus was recovered from these tumor cells or from tumors produced by them. Inoc. of 10³, 10⁴, 10⁵, transformed X1 cells from passage 11 produced tumors in 5/6, 6/6, and 6/6, resp., in 15 days; 10²-10⁴ X10 cells from passage 14 produced tumors in 23 days. Tumor incidence in controls which received 10³, 10⁴, 10⁵, normal hamster cells was 0/6, 0/6, and 4/6, resp., in 12 days. Metastases developed only in hamsters inoc. with transformed cells. Primary SV40-induced tumors were solid, less cellular and more slowly growing than those produced by transformed cells, although cell types were similar.

63-946 VIRUS OF AVIAN MYELOBLASTOSIS (BAI STRAIN A). XXIII. MORPHOLOGY OF VIRUS AND COMPARISON WITH STRAIN R (ERYTHRO-BLASTOSIS). (E.) Bonar, R. A. (Dept. Surg., Duke U. Med. Ctr., Durham, N.C.), U. Heine, D. Beard and J. W. Beard. *J. Nat. Cancer Inst.* 30(5):949-997, 1963.

Electron microscopic examination of preparations (made by various technics) of BAI strain A avian virus from the plasma of birds with myeloblastosis disclosed that the particles were spheroidal but easily distorted. The particles had a relatively firm inner granular or filamentous nucleoid structure surrounded by a thin membrane and an easily deformable outer layer covered by a membrane with knob-like projections. The 2 portions of the virus were separable by a variety

of physical and chemical methods. Strain R virus from the plasma of birds with erythroblastosis had the same morphology.

63-947 CORTISONE AND THYMIC EXTRACT IN MOUSE VIRAL LEUKEMIA. (E., Abstract)

Levinthal, J. D. (Harvard Med. Sch., Boston, Mass.) and M. D. Eaton. Proc. Am. Assn. Cancer Res. 4(1):30, 1963.

In newborn Ak x C3Hf/Gs hybrid mice inj. at birth with Gross passage A leukemia virus, monthly 3-day cortisone treatments (1 mg/day, starting at 4-9 wk., until death) did not change the frequency of leukemia, 92% of 24 in controls, 86% of 94 in treated mice. However, the median latency was lengthened in treated animals, being longer in those treated from earlier ages. In similarly inoc. mice thymectomized at 1 mo. of age, or thymectomy followed by inj. of heat-inactivated (56°C for 1 hr.) saline extracts of mouse thymuses from C57Bl, C57Br, or Swiss donors (weekly x 5 mo.) the frequency of leukemias decreased to 10% of 9 and 10% of 22, resp., from an intact control frequency of 85% of 27. Injection of fresh thymus extracts to either thymectomized or intact mice altered the frequency of leukemia to 21% of 24 and 21% of 19, resp.

63-948 COMPARATIVE RESISTANCE TO ACID OF THE POLIOMYELITIS VIRUS, OF HERPES, THE FOAMY AGENT AND OF SV40. (Fr.) Dubreuil, R. (Inst. Microbiol., U. Montreal, Canada), A. Chagnon and V. Pavilanis. Canad. J. Microbiol. 9(3):359-367, 1963.

Exposure of strains of poliovirus used in the production of the Salk or of the Sabin vaccine, human herpes, SV40 and "Foamy agent" (a known contaminant of poliovirus vaccine) to a wide range of pH under various conditions allowed selected survival of the polioviruses due to the marked resistance of all its strains to acid conditions. Specifically the SV40 was inactivated to less than 1% at pH 3.0 x 48 hr. at 5°C, or reduced 10⁶ x by exposure to pH 3.0 x 4 hr. at 37°C or to pH 2.5 x 48 hr. at 5°C. The treatment was effective on formalin-treated vaccine preparations containing 1% SV40 of a titer = 10^{6.0} cytopathogenic dose/50/ml.

63-949 IN VITRO CULTURE OF FRIEND'S VIRUS. (Fr.) Vigier, P. (Pasteur Lab., Radium Inst., Paris) and A. Goldé. Bull. Assn. Franc. Cancer 49(4):374-381, 1962.

Primary cultures of 12-18 day trypsinized Swiss or AKR mouse embryos, or secondary cultures from fibroblasts of the same, supported multiplication of Friend's leukemia virus in medium M 199 + horse and calf embryo serums. Virus was obtained from cultures infected with cell-free extracts from spleens of leukemic mice,

from trypsinized leukemic spleen cells, and with media from infected cultures. Small amounts of virus (about 1 infectious mouse dose/0.2 ml) was obtained at about 14 days after infection and Friend's leukemia developed in about one-half of the inoc. animals after long latent periods. A somewhat larger virus yield was obtained from cultures inoc. with whole cells from infected spleens, possibly due to multiplication of the leukemic cells. A total of 3/44 AKR and 22/96 Swiss mice inoc. with infected culture media developed Friend's leukemia. Among test Swiss mice there were also 2 reticulosarcomas, 1/2 associated with Friend's leukemia, 1/2 at 12 mo. after inoc.; 1 osteosarcoma developed at 3.3 mo. in an animal without Friend's leukemia (all came from cultures infected with Swiss mouse material). There were also 4 cases of hemorrhagic spleen necrosis, 2/4 in nonleukemic mice inoc. with material originating from Swiss mouse spleens. The cell cultures showed no cytopathic effects on virus infection.

63-950 ISOLATION OF A MURINE LEUKAEMOGENIC VIRUS P-LLV. (E.) Prececutti, A. (NCI, Bethesda) and L. W. Law. Nature (London) 198:801-803, 1963.

An additional leukemogenic virus, P-LLV, apparently obtained from the tissues of a 5.5-month-old C3Hf/Bi leukemic mouse is described and characterized. The mouse had received, at 10 days, s.c. inj. from a highly oncogenic S-polyoma virus variant. Cell-free extracts of a 20% suspension of leukemic tissues (Selas 02) were inoc. s.c. into newborn or adult mice (0.05 or 0.2 ml, resp.). The original isolate caused leukemias in 11/16 newborn BALB/c mice (mean latency 110 days) and in 3/6 newborn C3Hf/Gs mice (mean latency 133 days). Two selective passages were made from cell-free extracts of tissues from 2 BALB/c mice which developed leukemias at 85 and 86 days, resp. The first caused leukemias in 3/3 4-day-old C3Hf/Bi mice (mean latency 125 days), in 7/9 newborn BALB/c mice (mean latency 112 days) and in 0/2 C3Hf/Bi 1-month-old mice. The second selective serial passage caused leukemias in 9/14 newborn and in 2/5 1-month-old BALB/c mice (latency range 87-136 days). The original and passaged lymphocytic neoplasm was of near-diploid constitution, with a mode of 41 chromosomes. Nevertheless, it grew progressively in C3Hf/Lw, C3Hf/Fg, BALB/c, and DBA/2 mice, but not in C57BL and C57BR mice. A filtrate from the 4th generation transplants in C3Hf/Fg mice, and an ultracentrifugate from plasma were both found to be active. On growth of leukemic lymphoblasts from the original neoplasm in tissue culture, cells continued to produce leukemia on transplantation into C3Hf/Bi hosts throughout 6 mo. of continuous culture; and a Selas 02 filtrate from a 1 mo., but not from a 3 mo. culture, was active at a somewhat increased latent period. Observation of offspring born to infected mothers indicated that the virus is perpetuated and is transmitted to the progeny of leukemic mothers and inoc. mothers before their leukemia became manifest. Electron

Microscopic study of megakaryocytes from leukemic spleens showed type C particles. Animals inoc. with P-LLV either as newborn or adults usually contracted a widely disseminated lymphocytic neoplasm or an aleukemic thymic lymphosarcoma. The isolate presents many of the characteristics of the Moloney virus, which is in use in the author's laboratory. Further characterization is in progress, in order to determine whether P-LLV is in fact a new leukemogenic virus.

951 STUDIES ON THE KINETICS OF SV40 IN VITRO. (E., Abstract) Fernandes, M. V. (Inst. Wistar, Philadelphia, Pa.). Proc. Am. Soc. Cancer Res. 4(1):19, 1963.

Early after infection with simian virus 40 (SV40) of African green monkey kidney cells, hamster embryo cultures, and human diploid cell strains, the nucleoli appeared paler than those of control cells. Subsequently RNA material diffused throughout the nuclei and became concentrated around or within DNA positive inclusions. Cells with large but unswollen nuclei showed the first signs of infection. In the final phase of infection in monkey kidney cells, virus could be detected in the cytoplasm without previous rupture of the nuclear membrane. In all cells, cytoplasmic revacuolization was related to the lesions in the nuclei. In a human diploid strain, virus infection resulted in abnormal mitosis with unequal distribution of protoplasm and a peculiar arrangement of the mitochondria. During the process of cell division cytoplasmic fragments appeared to be extruded from the cells.

952 ONCOGENICITY OF SIMIAN VIRUS (SV40) AND ITS INACTIVATION WITH BETA-PROPIOLACTONE (BPL). (E., Abstract) Hayashi, (Dept. Labs., Henry Ford Hosp., Detroit, Mich.) and G. A. LoGrippo. Fed. Proc. 22(2):8, 1963.

Beta-propiolactone (BPL) inactivates simian virus (SV40) in tissue cultures and infected cell suspensions at 0.16% and 0.35% (wt./vol.), respectively. Combined BPL (0.35%) + UV (8-12 mw/cm²/sec.) treatment of extracts from rhesus monkey kidney (Rh-MK) cells containing SV40 resulted in no tumors 8 mo. after inoc. into 91 suckling hamsters. Untreated infected Rh-MK extracts caused fibrosarcomas in 41% of 120 suckling hamsters 8 mo. after inoc. Suckling hamsters, receiving treated transplants of tissues from primary tumors induced by SV40, developed tumors in 1/63 animals at 14-17 days, whereas 66 animals inoc. with transplants treated with 0.35% BPL had no tumors at 8 wk.

953 THE EFFECT OF HUMAN VIRUS PAPILLOMA EXTRACTS ON RABBIT ENDOTHELIAL PLANTS. (Rus.) Ptokhov, M. P. (Inst. Oncol.,

Acad. Med. Sci. USSR, Moscow). Vop. Onkol. 9(6):34-41, 1963.

5-7-day-old rabbit endothelial explants in medium 199 and human serum were treated with 2-3 drops of 10% human skin papilloma extract and were observed 1-175 days. During the first stage of cultivation the extract had cytotoxic effects upon the cells, but growth was maintained. After 2-3 days 10%-12% of the cells became basophilic, vacuolated and the nuclei and nucleoli decreased in size and stained more darkly. Cells which survived 7-9 days had enlarged nuclei and eosinophilic inclusions 1-10 μ in size. After 3-4 passages (30-40 days) the cells which survived became stabilized and cultures grew faster than the controls, which were treated with heat-inactivated extract. On days 70-80 the mitotic activity increased considerably (7-8 figures in one field), and the cells were found to be polymorphic and rich in nucleic acids. After admin. of the 10% extract (0.2 ml x 2) to CC57 mice, only 1/200 had developed a mammary tumor after 11 mo. After 14 mo. there were 37 survivors.

63-954 REACTION TO THE LEUKEMIC VIRAL-ANTIGEN IN GUINEA PIGS INOCULATED WITH HUMAN MYELOID LEUKEMIA. (Sp.) Mas y Magro, F., Jr. (Inst. Hematol. Exptl. Cytology, Alicante, Spain). Sem. Med. (B. Air.) 122(6):161-164, 1963.

Inoc. of guinea pigs (by scarification) with dried blood from pts. with acute or chronic leukemia resulted in short-term death of 90% of those inoc. with material from pts. with the acute form. Specific leukemic changes in survivors included the appearance of atypical promyelocytes (demonstrable by the peroxidase reaction) and eosinophilia, demonstrable in all inoc. animals, including the survivors. In 4 guinea pigs inoc. with leukemic material (1/4 from chronic, 1/4 granulocytic, and 2/4 from acute myeloid leukemia), eosinophilia was followed in detail. By day 11-13 eosinophils had increased to 31%-39% in 3/4, in 1/4 increase was observed on day 94. There was a further gradual increase up to a max. of 96% in 1 animal. The eosinophil increase paralleled the increase in WBC (28,000-146,800/mm³) and persisted for up to 1100 days in 1 case. Re-activation was obtained in 2/4 by trauma (breakage of limb), by pregnancy in 1/4, and by intense asthenia leading to death in 24 hr. in 1/4 (marrow showed intense eosinophilia). It is concluded that the eosinophilia is a reaction to an antigen presumed to be the virus of human leukemia.

63-955 THE RECOVERY OF INFECTIOUS NUCLEIC ACID FROM A VIRUS-INDUCED LYMPHOID NEOPLASM. (E.) Moloney, J. B. (NCI, Bethesda). Acta Un. Int. Cancr. 19(1-2):250-251, 1963.

A protein-free phenol + bentonite extract of pooled spleens, thymuses, and lymph nodes from BALB/c and Osborne-Mendel rats with leukemias

induced by inoc. of the lymphoid-leukemia virus (Moloney) from Sarcoma 180, were analyzed for infectivity and type of nucleic acid. In newborn BALB/c rats inj. with the extract (0.02 ml intracranially or 0.1 ml s.c.) the frequency of lymphoid leukemias was 11.8% with a latency of 4.5-6.0 mo. The spontaneous frequency of lymphoid leukemias is 1.0% in the BALB/c strain. The leukemias induced by inj. of the nucleic acid resembled histologically those caused by the intact virus, and the same type C viral particles were observed within the cytoplasmic channels of bone marrow cells. The nucleic acid-induced leukemias were transmissible as cell-free extracts to newborn BALB/c rats, where the frequency was about 12%, with a mean latency of 2 mo. Incubation of the nucleic acid fraction with RNase destroyed infectivity, whereas DNase treatment was ineffective.

- 63-956 TIME-LAPSE CINEPHOTOMICROGRAPHY OF CHICK CELLS INFECTED WITH ROUS SARCOMA VIRUS. (E., Abstract) Dougherty, R. M. (Upstate Med. Ctr., Syracuse, N.Y.) and D. J. Trevan. Proc. Am. Assn. Cancer Res. 4(1):17, 1963.

Under phase contrast, time-lapse cinematography of chick embryo fibroblasts in cell culture infected with Rous sarcoma virus showed in early stages marked alterations at the cell surfaces with later rounding of cells. Subsequently, most of the cells in a transformed focus showed bubbling resembling that observed during mitosis of normal cells. The bubbling persisted throughout the life cycle, including interphase. In the transformed foci mitosis continued after it had ceased in the surrounding normal-appearing cells.

- 63-957 IN VITRO MULTIPLICATION AND MORPHOLOGIC ALTERATION OF RABBIT KIDNEY CELLS INFECTED WITH FIBROMA VIRUS. (E., Abstract) Hinze, H. C. (Dept. Med. Microbiol., U. Wisconsin, Madison) and D. L. Walker. Fed. Proc. 22(2):557, 1963.

Serially cultured rabbit kidney epithelial cells infected with sufficient fibroma virus to infect 100% of the cells in 24-48 hr. and maintained under optimal growth conditions for 2-3 wk. were able to multiply to a degree exceeding that of uninfected controls. The infected cultures also demonstrated cell morphology and growth patterns distinctly different from those of uninfected control cultures. The carefully controlled conditions of temperature and nutrition are considered responsible for the cell proliferation observed, since rabbit kidney cells maintained under the usual laboratory conditions usually respond to fibroma infection with viral multiplication accompanied by gradual degeneration of the cultures.

- 63-958 QUANTITATIVE STUDIES ON THE DEVELOPMENT OF FRIEND'S DISEASE IN TWO INBRED STRAINS OF MICE. (E., Abstract) Bostick, W. L. (U. Calif. Med. Sch., San Francisco) and F. C. Ludwig. Fed. Proc. 22(2):314, 1963.

Groups of 3 month-old RF or BALB/c mice were inoculated with an ID₅₀ of Friend's disease virus (FDV) and sacrificed at intervals of 2-80 days after virus inoc. In both mice strains FDV caused a 25% increase in the nucleated marrow cell count, which reached a plateau by wk. 3. In the BALB/c strain the appearance of the leukemic blood picture was correlated with a sharp rise in mortality to 100%, whereas in the RF strain, which was aleukemic, mortality rose only to 50%. Study of organ wt. and histopathologic changes suggests that the leukemic cells of the peripheral blood are of splenic origin.

- 63-959 BLOCKING EFFECT OF WEST NILE VIRUS ON PRODUCTION OF SARCOMA BY ROUS VIRUS. (E., Abstract) Shirodkar, M. V. (Virus Res. Ctr. Poona, India). Fed. Proc. 22(2):439, 1963.

West Nile virus (WNV, Egypt 101 isolate) inoc. bilaterally or unilaterally into wing webs of White Leghorn chicks of different age groups blocked tumor production by Rous sarcoma virus (RSV; "V" strain) inj. bilaterally at the same site, or contralaterally. The blocking effect ranged from total prevention to prolonged latency of sarcoma formation. Birds protected against the tumor by WNV showed no antibodies to RSV. Little or no oncolysis was apparent when RSV preceded WNV by 24 hr.; prolongation of latency occurred when both viruses were admin. simultaneously; increasing blockade of tumor formation was observed on delay of the RSV inj. 24-144 hr. At 144 hr. total prevention of sarcoma was observed in 30% of chicks. This protective effect disappeared by 240 hr. Preliminary *in ovo* experiments failed to demonstrate interferon-like substance(s) active against RSV-induced sarcomas, although the chorio-allantoic fluid of WNV-injected embryos contain some inhibitor(s) against WNV.

- 63-960 TOXICITY IN CHICK EMBRYOS PRODUCED BY BLOOD OF TUMOR-BEARING ANIMALS. (E., Abstract) Handler, A. B. (Children's Cancer Res. Foundation and Harvard Med. Sch., Boston, Mass.) and S. Farber. Proc. Am. Assn. Cancer Res. 4(1):26, 1963.

Blood and plasma samples from a variety of animals with several types of generalized leukemia or of metastasizing malignant solid tumors were toxic to chick embryos when inoc. into the chorio-allantoic membrane of 7-9-day-old eggs. Whole blood and plasma were not toxic to chick embryos when obtained from normal White Leghorn chickens, 6 strains of mice, Syrian hamsters, guinea pigs, dogs, W/Fu rats, and rabbits,

animals with benign tumors; spontaneous, induced and transplanted non-metastasizing malignant tumors; mice and hamsters in various stages of pregnancy; postnatal mice and hamsters; and animals inoc. with carcinogens.

3-961 REDUCTION IN THE FRACTION OF C3H LYMPHOMA CELLS CAPABLE OF PROLIFERATION IN HOSTS TREATED WITH GROSS' VIRUS EXTRACT. (E., Abstract) Axelrad, A. A. (Dept. Med. Biophys., U. Toronto, Canada). Proc. Am. Assn. Cancer Res. 4(1):3, 1963.

Injection of 10⁷ viable murine lymphoma cells into C3Hf/BI mice treated with a single dose of Gross Passage A virus extract resulted in a significantly lower number of spleen colonies than observed in untreated controls. Inhibition of spleen colony formation could also be brought about by pretreatment of hosts with sublethal doses of viable lymphoma cells. Results are compatible with the concept that growth of Passage A virus-induced C3H lymphoma cells is resisted by an immune response of C3H hosts directed against foreign antigen(s) on the cells.

3-962 HEMORRHAGIC DISEASE INDUCED IN YOUNG RATS BY ROUS CHICK SARCOMA VIRUS. (E.) Sokoloff, B. (A. P. Cooke Mem. Cancer Lab., Florida Southern Coll., Lakeland), K. Nomoto, C. C. Saelhof, M. Fujisawa and L. Bird. Growth 27(1):29-38, 1963.

When Rous chick sarcoma virus (RSV, diluted 1:2) was inoc. prenatally (0.1 ml 10-12 days before birth) to rat embryos or inoc. both pre- and postnatally (0.2 ml x 3, s.c.), hemorrhagic disease (HD) developed in 75% and 95%, resp.; mortality rate was 33% and 40%, resp.; and the number of hemorrhagic sacs per square cm of skin was 12.3 and 16, resp. HD did not develop in rats inoc. with inactivated RSV. Ascorbic acid given orally to pregnant, treated rats (50 mg/kg/day x 22) and to postnatal rats (25 mg/kg/day x 55) led to nonsignificant reduction of HD (55% and 78%, resp.); mortality was 25% and 33%, resp. Similar treatment with bioflavonoids (100 mg/kg/day x 22 for pregnant rats, 50 mg/kg/day x 55 for postnatal rats) led to a reduction of HD (28.7% and 34.8%, resp.); mortality was 12.5% and 11%, resp. The hemorrhagic lesions revealed the presence of capillarotoxicosis; evidence of inflammatory process was apparent. All attempts to detect RSV in the hemorrhagic sacs or tissues were negative. The complement fixation test for RSV antibodies in rat serum was negative except for 8/28 of the pre- and postnatally RSV-treated rats who received bioflavonoids after birth.

3-963 A COMPARATIVE STUDY OF PATHOLOGICAL PROCESSES IN MAMMALS CAUSED BY THE ROUS VIRUS. (E.) Svet-Moldavsky, G. J.

(Inst. Exptl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). Acta Un. Int. Cancr. 19(1-2):299-301, 1963.

Rous sarcoma virus (RSV) inoc. into embryonic or neonatal albino rats produced a peculiar cystic exudative hemorrhagic disease with relapses and remissions followed by development of polymorphic sarcomas rich in mucoid substance, or, after recovery, solid homogeneous fusiform cellular sarcomas. Neonatal inoc. of RSV into cotton rats (Sigmodon hispidus hispidus), which develop more rapidly, induced sarcomas not preceded by the hemorrhagic disease. Although RSV could sometimes be isolated from rat sarcomas, it was not established whether the sarcomas resulted from the direct malignant transformation of rat cells by the virus or from the secondary nonvirus malignant processes occurring in the cysts. It is pointed out that the cyst walls consist of parallel rows of fibroblasts, and that the condition resembles histologically that observed during sarcoma induction by implantation of plastic plates. The author suggests that the mechanism of this development may differ in the two types of sarcomas.

63-964 ON THE ONCOGENIC ACTION OF MONKEY KIDNEY TISSUE CULTURE PREPARATIONS. (E.) Deichman, G. I. (Inst. Exptl. Clin. Oncol., Moscow) and E. L. Prigogina. Acta Un. Int. Cancr. 19(1-2):334-335, 1963.

Supernatants from monolayers of Macacrus rhesus and M. cynomolgus kidney cells infected with extracts of human mammary cancer for 7-25 days were inoc. into newborn rats; tumors appeared in 11-24 mo. equally divided between experimental and controls. No correlation could be found between tumor incidence, human material used, or number of passages in vitro; no oncogenic virus was recovered from the rat tumors using mouse, rat or human tissue cultures. Of 26 newborn hamsters inoc. with medium from the same monkey kidney cultures, 40% developed multiple sarcomas at the site of inoc. in 4-6 mo.; simian virus (SV40) was isolated from 5/6 of the Rhesus kidney cultures, from extracts of 2/5 of the induced tumors, the urine of 2/2 tumor-bearing hamsters and from the spleen of the 1 F₁ progeny of the infected animals tested, but not from 6 kidney cell cultures of tumor-bearing hamsters or 3 tumor extracts of rats given Rhesus monkey kidney cultures. It is concluded that tumors appearing in hamsters were definitely attributable to SV40, but that the relation of SV40 to the rat tumors remains unclear.

63-965 NON-RANDOM CHROMOSOMAL ABERRATIONS IN SV40-ALTERED HUMAN CELLS. (E., Abstract) Moorhead, P. S. (Wistar Inst., Philadelphia, Pa.), E. J. Saksela and F. C. Jensen. Proc. Am. Assn. Cancer Res. 4(1):45, 1963.

Cell strains from 8 buccal and skin biopsies of 4 cancer pts. were analyzed karyologically following infection in vitro with simian virus SV40. Significantly frequent were eliminations of members of the acrocentric groups 13-15 and 21-22, and also of 17 and 18. Involvement of chromosomes numbers 1, 4-5, 13-15 in dicentric formation and in other arrangements was often noted. Abnormal stretching and breakage at specific secondary constrictions were prominent. The human diploid cell strain WI-38 and a trisomic-21 strain (Pall.) also showed similar abnormalities when infected after many passages in vitro.

63-966 ROUS SARCOMA IN MAMMALS. (E.)
Ahlström, C. G. (Inst. Path., U. Lund, Sweden), S. Bergman, N. Forsby and N. Jonsson.
Acta Un. Int. Cancr. 19(1-2):294-298, 1963.

Cellular or cell-free material from chickens with Rous sarcoma virus (RSV) induced sarcomas in a variety of other species with the following characteristics: young rats, spindle cell in 50-75%, in 4-5 wk., with frequent hemorrhagic cysts in lymph nodes; newborn mice, sarcomas in 25% in 3-12 wk.; hamsters, polymorphous sarcomas, within 4 wk. in newborn, and 7 mo. in adults; young guinea pigs, spindle cell sarcomas, sometimes regressing, others metastasizing to lungs, in 3-4 wk.; young rabbits, fibrosarcoma-like tumors, in 2-3 wk., always regressing, and also with lymphogenic cysts. The rat sarcomas were passaged successfully 32 x, yielding RSV at all passages tested except 6 and 28. The mouse tumors were passaged 22 x, with virus absent at passages 13, 21, and 22. The hamster tumors were passaged 7 x, with virus in all but 2 and 3. Guinea pig tumors passaged up to 4 x failed to yield RSV, and the rabbit tumors did not transplant and failed to yield virus. The rat and fowl sarcomas had no common antigens, and chromosome patterns of tumors from various species were those of the resp. host. In tissue cultures of embryonal fibroblasts from rats, guinea pigs, mice and chicks, the RSV caused foci of granulated cells at about 9 days. The effects of this RSV (isolated from a typical sarcoma by Schmidt-Ruppin) differed from that of the Mill Hill strain which does not induce tumors in newborn rats and mice, and produced granulation lesions only in chick fibroblast cultures. However, serologic studies in progress indicate cross immunization of the 2 strains.

63-967 AN ANTIGENIC ANALYSIS OF RAT KIDNEY TUMORS INDUCED BY POLYOMA VIRUS, AND

OF NORMAL TISSUES IN VIVO AND IN VITRO. (E.)
Fogel, M. (Weizmann Inst. Sci., Rehovoth, Israel).
Acta Un. Int. Cancr. 19(1-2):175-180, 1963.

Antisera to normal albino rat kidney absorbed with normal liver mitochondria + rat kidney tumor (from polyoma virus inoc., Toronto strain) reacted only with normal kidney, whereas antisera to the kidney tumor, absorbed with normal kidney and normal liver mitochondria reacted with kidney tumor and also, to a somewhat lesser extent, with embryo and normal kidney cultures and with kidney tumor cultures. Antisera prepared from cytoplasmic particles of 6-day rat embryo cultures, absorbed on kidney and kidney tumor reacted only with all three tissue cultures, whereas they reacted with tumor and all three tissue cultures when absorbed on normal kidney + normal embryo antigen. Antisera to 6-day cultures of kidney tumor reacted with tumor and with all three tissue cultures after absorption on kidney + normal lung. It is suggested that some cells grown in tissue cultures undergo changes which may be similar to changes which occur in tumor cells growing in vivo.

63-968 THE DISTRIBUTION OF POLYOMA VIRAL ANTIGEN AS DETECTED BY IMMUNOFLOUORESCENCE IN THE TISSUES OF INFECTED MICE. (E.)
Levinthal, J. D. (Dept. Bacteriol., Harvard Sch. Med., Boston, Mass.), B. Takacs and M. D. Eaton.
Acta Un. Int. Cancr. 19(1-2):318-321, 1963.

Immunofluorescent study of tissues of 80 polyoma virus (PV; Toronto SE or the authors' own strain) infected Swiss mice and C₃H_f/Bi baby mice revealed that the earliest site of replication was the skin, then renal mesenchyme followed by tubule cells, cells of the auricle, periosteum, bone marrow, biliary epithelium, blood vessels, thyroid, salivary gland capsule, thymus and other tissues. Phagocytic cells containing cytoplasmic clumps of antigen appeared in lymph nodes and liver sinuses. With moderate doses, cells with viral antigen tended to disappear abruptly during wk. 2; with doses lethal at 2-7 wk., chronic lesions appeared. It was concluded that PV propagated in tissues in which tumors later appeared; a high local conc. of virus was achieved by lysis and release of PV from infected cells; transformation probably occurred at this time. It is suggested that for tumor induction, it may be necessary for a sufficiently large number of transformed cells with new antigen to appear in the brief period after birth in which tolerance to foreign antigens may be established. Similar studies of 49 primary tumors in 27 tumor-bearing C₃H_f/Bi or AK/C₃H hybrids revealed that viral antigen rarely appeared in PV-induced tumors.

See also abstract nos.: 792, 793, 794, 802, 803, 805, 833, 836

EPIDEMIOLOGY AND BIOMETRY

3-969 THREE CASES OF GASTRIC CARCINOMA IN A FAMILY SEEN IN A SHORT PERIOD OF TIME. (Jap.) Matsuoka, K. and R. Nakaya. Gan no Shinsho (Jap. J. Cancer Clin.) 9(1):48-52, 1963.

Gastric carcinomas were found during operation in a father, age 65 yr. and 2 daughters, ages 5 and 30 yr. Duration of symptoms was about 5 mo. in the father and 1 daughter, and about 1 yr. in the 2nd daughter. The father's tumor was a spindle cell carcinoma, situated around the lesser curvature and cardiac end of the stomach, with lymph node and liver metastases. He died about 3 mo. after surgery. The tumors of both daughters were carcinoma simplex found, in the pyloric area. Both recovered after surgery and were living at the time of report.

3-970 DERMATOLOGIC ASPECTS OF ONCOLOGY IN THE WORK OF THE NATIONAL ONCOLOGIC INSTITUTE. (Hun.) Venkei, T. (Derm. Dept., Nat. Oncol. Inst., Budapest). Borgyogy. Vener. szemle 38(6):244-249, 1962.

According to the statistics of the Nat. Oncol. Inst., 18-20,000 new cases of malignant tumor were discovered yearly (in a population of 10 million) in Hungary. The observed increase in the number of cases is ascribed to the general prolongation of the life-span, improvement in diagnosis and compulsory registration, and an actual increase in the incidence of certain types of malignancy, such as cancer of the lungs, leukemia, reticulosarcoma, and melanoblastoma. In 1959, approx. 17% of the cases of malignancy in the Institute's case material were skin tumors; another 6% were labial carcinomas and oral cancers which could be diagnosed early by dermatologists. Furthermore, in some 23% of the remaining cases of cancer, dermatologic signs figured in the clinical picture. The diagnostic implications of these statistics are discussed, and various special technics are proposed for the early identification of precancerous and cancerous lesions, especially in the case of workers exposed to radiologic or radioactive materials and dangerous chemicals. It is considered most important to deal with the problems of the etiology, pathogenesis, diagnosis and treatment of melanoblastomas and keratoacanthomas.

3-971 RADIATION THERAPY IN THE TREATMENT OF CARCINOMA OF THE LUNG. (E.) Hurr, R. C. (Queen's U., Kingston, Ontario), E. N. MacKay and A. H. Sellers. Canad. Med. Assn. J. 88(24):1181-1184, 1963.

In the past 25 years the death rate from cancer in Ontario has increased 9 fold for males; 2 fold for females. The male:female ratio varied from an av. of 8.5:1 to as high as 11.7:1 at the ages of 65-69. For males the ratios expressed as percentage of actual deaths expected at the age

specific rates for all Ontario were 145 for cities of 100,000 and over; 112 for cities of 35,000-100,000; and 79 for the remainder of the province. Of 2457 lung cancer pts. registered at the Ontario Cancer Clinics (1937-58), 73% were pathologically confirmed; half were squamous cell carcinomas. Survival in relation to treatment was also discussed; improvement in results may be attributed to the difference in treatment employed.

63-972 GEOGRAPHIC DISTRIBUTION OF LEUKEMIA. (E.) Abernathy, E. L. (Wash. Hosp., Wash. County, Pa.). Med. Bull. Wash. County Med. Soc. 56(6):8-10, 1963.

A preliminary study of 246 cases of malignant blood dyscrasias seen at Washington Hospital, Pa., between 1932-1962 revealed 57 to be acute blastic leukemia, 36 chronic myelogenous, 38 Hodgkin's disease, 31 chronic lymphocytic leukemia, 29 polycythemia vera, and 55 miscellaneous types. Geographically, the largest incidence of leukemia was in areas of high density population. However, 3 cases of the same type of leukemia occurred on the same street within 5 yr., with 3 more cases nearby in an area of normal population density. The incidence of acute blastic leukemia in 2 northwestern communities was approx. twice the expected incidence given in standard texts and was out of proportion to the known population. Incidence of pancreatic carcinoma was also high.

63-973 SURVIVAL IN HODGKIN'S DISEASE. (E.) Meighan, S. S. (Dept. Public Health, Regina, Saskatchewan, Canada) and J. D. Ramsay. Brit. J. Cancer 17(1):24-36, 1963.

In a survey of Hodgkin's disease in Saskatchewan, covering all cases reported between 1946 and 1960, 150 cases were discovered, giving an incidence (per 100,000) of 1.62/yr. In the series, 6/150 were Hodgkin's paraganulomas; the remainder, classical cases of Hodgkin's disease. The male to female ratio was 2.06:1. The greatest number of pts. were in the 20-29 age groups, with a median age for all pts. of 35 yr. However, when the age distribution of the corresponding population was taken into account, the incidence of the disease showed a clear-cut, bimodal curve with peaks at 20-29 and at 70 yr. or over. Using a 5-yr. cut-off time to increase statistical meaningfulness, the median survival for pts. in this series was 26.5 mo. and the mean was 30.6 mo., with 32% surviving >5 yr. from the time of diagnosis.

63-974 PRIMARY CARCINOMA OF LIVER WITH SPECIAL REFERENCE TO HISTOGENESIS AND ITS RELATIONSHIP TO LIVER CIRRHOSIS. (E.) Ying Yüeh-Ying (Dept. Pathol., Shanghai 1st Med. Coll., China), Ma Cheng-Chung, Hsü Yuan-Ting, Lei Hsüeh-Hsi, Liang Shu-Feng, Liu Ch'ien-Hsin and Ku Ching-Yen. Chin. Med. J. 82(5):279-294, 1963.

In the period 1938-1960, in Shanghai among 3,498 general autopsies, 107/567 malignancies were primary liver carcinomas amounting to 18.9% of the malignancies and an incidence of 3.06%. The male:female ratio was 5:1; of the 107 cases, 98 were males and 9 were females. Most of the cases were found in the age group 45-49, which is 10 yr. younger than in Europeans and 10-20 yr. older than in the Africans. The process of cancerous transformation involved a considerable degree of liver parenchyma destruction, proliferation, and anaplasia of proliferating cells. It is concluded that liver carcinomas of 3 types can be formed from the proliferation of either liver or bile cells. Primary carcinoma of the liver was associated with liver cirrhosis in 89 cases; 56 were of the portal type; 18 of the mixed type; and 15 the postnecrotic type. Cirrhosis was most often associated with liver cell carcinoma and least often with bile duct carcinoma. Viral hepatitis was an etiological factor in postnecrotic and mixed types of cirrhosis. Schistosomiasis of the liver was found in 17 cases causing varying degrees of liver cirrhosis. Nutritional deficiency, alcoholism, and *Clonorchis sinensis* infestation did not appear to be etiological factors. It is concluded that cancerous changes can occur only in those types of cirrhosis in which there is active proliferation of liver or bile duct cells.

- 63-975 EOSINOPHILIC INFILTRATION AND GRANULOMA OF THE GASTROINTESTINAL TRACT. (Hun.) Hollosi, K. (Dept. Pathol. Anat., István Munic. Hosp., Budapest) and G. Nagy. *Orv. Hetil.* 104(11):496-500, 1963.

On the basis of the 3 cases described (all undergoing a Billroth II operation for suspected gastric polyps and/or tumor), the authors discuss the histologic picture of eosinophilic granuloma and infiltration of the gastrointestinal tract, which they regard as of probable allergic origin. Although the process evolves in some respects like a tumor, it is significantly different in other aspects. On the basis of data in the literature, and anamnestic clinical, and morphologic evidence, it does not appear likely that the condition is related to other allergic conditions, including collagen diseases, allergic angitis, allergic lymphadenopathy, etc.

- 63-976 THE PROBLEM OF THE MALIGNANT TRANSFORMATION OF PIGMENTED NAEVI. (Hun.) Szalay, E. (1st Pathol. Anat. Exptl. Cancer Res. Inst., Med. U. Budapest). *Magy. Onkol.* 7(1):25-32, 1963.

Observations on 162 pts. (114 female, 48 male, aged 0-60+ yr.) confirmed the significance of junctional activity (JA). Of the 162 nevi subjected to histologic study, 4 (2.5%) were epidermal, 7 (4.3%) complex, and 151 (93.2%) intradermal. Of the latter, 120 (74.1%) were purely intradermal, 17 (10.5%) showed low-grade JA, and 14 (8.6%) showed pronounced JA. The

frequency of JA was highest (21/26 or 8:10) in the youngest pts. (aged 0-9 yr.), and was progressively lower with increasing age (1/30 in pts. aged 50-59 yr.). The comparative incidence of JA and malignant melanoma was 8:10 and 0, resp., in 26 pts. aged 0-9; 1:2 and 1:20 in 17 pts. aged 10-19; 1:7 and 1:6 in those 30-39, and 1:30 and 1:3 in those aged 50-59. Malignant transformation was observed in epidermal and complex nevi and was most frequent in junctional and complex types, but it was never observed in purely intradermal nevi. Since repeated trauma is frequently associated with malignant transformation, nevi exposed to frequent irritation should be surgically removed as early as possible.

- 63-977 PROPOSAL FOR A CASE-SHEET PERTAINING TO THE LEUKEMIC CHILD. (It.) Fischer, F. (Inst. Puericult., U. Rome). *Arch. Ital. Pediat.* 22(3):256-260, 1962.

In order to facilitate etiological investigations and statistical studies, the author proposes and discusses in detail a uniform case-sheet for recording the anamnestic, etiological and environmental data in every case of childhood leukemia. Among other matters, the record would include data on hereditary diseases in the family, and irradiation of the mother and child.

- 63-978 LEUKEMIA AMONG CHILDREN IN A SUBURBAN COMMUNITY. (E.) Heath, C. W., Jr. (Tufts Hemat. Lab., Boston City Hosp., Mass.) and R. J. Hasterlik. *Am. J. Med.* 34(6):796-812, 1963.

Between 1957 and 1960, 8 cases of leukemia occurred among children living in one residential area of Niles, Illinois bringing the annual incidence (per 100,000) among children to 21.3 for Niles compared to 4.6 for the remainder of Cook County. Since 7/8 were from Roman Catholic families, whose children attended the one parochial school (PS), the incidence for this group was significantly increased to 59.8 ($P = 0.04$) compared to 7.1 for all other families. Of the 8 cases, 5 were stem cell leukemia, 1 lymphoblastic leukemia, 2 acute lymphocytic leukemia (1/2 with lymphosarcoma). Dates of onset of cases of leukemia and of "rheumatic-like illness" in 8 children associated with the PS were observed in 2 periods, Fall 1957-Spring 1958 and Fall 1959-Summer 1960. Within the same community there were 3 cases of acute leukemia in adults and 3 cases of cancers in children, all in Roman Catholic families although in only 60% of the area, families were Roman Catholic. An unusually high childhood mortality associated with congenital heart disease was also observed, with cases limited to Roman Catholic families.

- 63-979 RELATION OF BLOOD GROUPS A, B, AND O TO CARCINOMA OF THE STOMACH IN SÃO PAULO. (E.) Branco Ribeiro, E. (St. Luke's Sanitorium, São Paulo, Brazil). *J. Int. Coll. Surg.* 39(6):540-546, 1963.

used on blood donor data from 2 São Paulo institutions, the distribution of blood groups in the general population is calculated as 44.5% for 0, 39.9% for A, 12% for B and 3.6% for AB. The distribution among 100 pts. operated upon for gastric cancer is 35% of 0, 53% of A, 8% of B and 4% of AB. A significant increase in the incidence of Group A was apparent, the change due chiefly to the decreased incidence of Group 0. The Rhesus-positive to negative ratio was 922:0.078 among gastric cancer pts. as compared to a ratio of 0.906:0.094 for the general population. The author also reviews various studies on the relation of blood groups to gastric cancer.

-980 FOLLOW-UP STUDIES ON AN UNSELECTED TEN-YEAR MATERIAL OF 360 PATIENTS WITH PORTAL CIRRHOSIS IN ONE COMMUNITY. (E.) Hällen, (Dept. Med., General Hosp., Malmö, Sweden) and H. Krook. *Acta Med. Scand.* 173(4):479-493, 1963.

Primary carcinoma of the liver was found in 1/280 (11%) of the autopsy cases from a larger series of 360 pts. studied retrospectively. The male:female ratio was 4:1, and mean age 67. There was an equal frequency of cancers in the series in cirrhosis of alcoholic etiology (8% of 122), as in that due to hemochromatosis (7% of 8), or of cryptogenic etiology (11% of 5), suggesting that carcinoma develops with equal frequency in different types of cirrhosis.

-981 EDITORIAL. TUBERCULOSIS AND CANCER. (E.) *Brit. Med. J.* 1:1430, 1963.

The inverse relationship between mortality from tuberculosis and cancer of all types is discussed briefly. Data relating specifically to an increase in lung cancer risk with decreased risk of tuberculosis are still incomplete, however, four possible explanations are offered for the phenomenon. The first is that in pts. with healed tuberculosis, the residual scarring and metaplasia of the bronchial mucosa may open a way for malignant change. The second and third are based on an unspecified protective mechanism of tuberculosis on cancer, or on a genetic linkage of tuberculosis and cancer. The fourth, which is considered more likely, is that an increase in the standard of living and therapeutic effectiveness have coincided with the extension of coal-burning urbanization and a decrease in cigarette consumption.

-982 ACUTE YELLOW ATROPHY, CIRRHOSIS, AND HEPATOMA; THEIR INCIDENCE AT THE JOHNS HOPKINS HOSPITAL 1917-1960. (E.) Miyai, K. (Dept. Path., Johns Hopkins Sch. Med., Baltimore, Md.) and B. H. Ruebner. *Arch. Path. (Chicago)* 66(6):609-617, 1963.

A review of 25000 necropsies (1917-1960, Johns Hopkins Hospital) revealed 466 (1.86%) cases of

hepatic cirrhosis, 72 cases (0.29%) of hepatoma, and 46 cases (0.18%) of acute yellow atrophy. The estimated necropsy incidence of primary hepatic carcinoma was 0.46% for white males, 0.45% for Negro males, 0.07% for white females and 0.06% for Negro females. Of 72 pts. with hepatic cancer, 65 (90%) were males. In this group 43 (59.8%) also had cirrhosis, and therefore hepatic carcinoma complicated cirrhosis in 43/466 cases (9.3%). The average ages of hepatic cancer pts. with and without cirrhosis were 57.7 and 55.7 yr., resp. Eight cancer pts. (3 females, 5 males) had cholangiocarcinomas, none with coexisting cirrhosis. Hepatocellular carcinoma was present in the remaining cancer cases, complicating postnecrotic cirrhosis in 25/177 (15.0%) and portal cirrhosis in 10/243 (4.1%), while in 8 more cancer cases, the type of cirrhosis could not be determined due to extensive tumor invasion. After corrections were made for age and sex, it is apparent that the frequencies for portal cirrhosis, postnecrotic cirrhosis, and hepatoma, resp., have risen from 0.5, 0.3 and 0.5% in 1920-1925 to 0.7% for all 3 in 1940-1945, to 2.2, 1.0 and 1.2% in 1945-1950 and to 1.6, 0.9 and 0.8 in 1955-1960. Hepatoma and postnecrotic cirrhosis shared some epidemiologic features such as similar racial incidence, and a slight rise since 1930, compared to a greater rise for portal cirrhosis.

63-983 METHODOLOGICAL PROBLEMS AND DESIGN OF THE TRISTATE LEUKEMIA SURVEY. (E.) Graham, S. (Roswell Park Mem. Inst., Buffalo, N.Y.), M. L. Levin, A. M. Lilienfeld, J. E. Dowd, L. M. Schuman, R. Gibson, L. H. Hempelmann and P. Gerhardt. *Ann. N. Y. Acad. Sci.* 107(2):557-569, 1963.

The design of a retrospective tristate (New York State outside New York City, Baltimore, and Minneapolis-St. Paul and surrounding rural areas) survey of leukemia, both chronic and acute in adults and children over a 4-year-period is detailed. It is believed that completion and evaluation of the data will shed some light on the epidemiology of leukemia.

63-984 EDITORIAL. REDUCTION IN CANCER MORTALITY AMONG WOMEN. (E.) *Statist. Bull. Metropolitan Life Insur. Co.* 44:1-3, 1963.

Mortality from malignant neoplasms of various sites among white female industrial policyholders are compared for the yr. 1950-1951 and 1960-1961. Cancers of 2 sites, uterus and intestine, have shown the greatest absolute decreases over the decade studied (-46 and -21% for ages 1-74), whereas cancer of the lung and bronchus has shown a relative increase (+20% for ages 1-74), and cancers of the pancreas, breast, brain, and leukemia have shown an increase in some age groups, and a decrease in other age groups. For uterine cancer, ages 1-74 yr., the av. death rate (per 100,000) in 1960-1961, and its percentage change from the death rate in 1950-1951 was 6.7 (-46%), with incidences of 8.2-47.5 on increasing age from 35-74 yr.; the decreases ranged from -41%-53%

in age groups over 35 yr. For intestinal cancer corresponding figures were: 1-74 yr., 7.2 (-21%), with higher incidences of 14.9-77.5 in age groups 45-74, but with reductions of -8 to -28% in all age groups over 35 compared to 1950-51. For breast cancer, with a total incidence at 1-74 yr. of 14.0 and reduction of -2%, and incidences of 19.3 to 84.0, increasing with age, there were decreases of -3 to -8% in all age groups over 35 yr. with the exception of ages 45-54 where there was a change of +4%. Cancers of the rectum, biliary passages + liver, stomach, and ovary with incidences for ages 1-74 yr. of 2.4 to 4.6, all decreased -10 to -48%, with decreases observable in all age groups. In cancer of the brain, ages 1-74 yr., 1.9 (-17%), there were increases of +13 and +31% in age groups 55-64 and 65-74, resp. For leukemias, ages 1-74 yr., 3.7 (-7%), there was, however, an increase of +27% in age group 65-74. For cancer of the pancreas, 1-74 yr., 2.4 (-8%) there were increases of +86% in age group 35-44. Cancers of the lung + bronchus, ages 1-74 yr., 3.0 (+20%) rate increased in frequency from 1950-1961 as follows: 35-44, 2.7 (+29%); 45-54, 8.8 (+66%); 55-64, 13.9 (+16%); 65-74, 25.8 (+1%).

- 63-985 DERMATOMYOSITIS AND BRONCHOGENIC CARCINOMA. (E.) Montes, L. F. (Derm. Ser., Fernandez Hosp. Buenos Aires, Argentina), E. F. Lascano, O. Alva, F. Doreski and M. A. Mazzini. *Arch. Derm. (Chicago)* 87(5):637-640, 1963.

After presentation of a pt. with dermatomyositis with later discovery of bronchogenic carcinoma, the authors review a series in which there is the same association. Many investigators feel that dermatomyositis associated with cancer could represent an autoimmune reaction, with muscle as the shock organ. In the case reported, the sequence of events seemed to indicate the presence of an autoimmune mechanism.

- 63-986 ORAL CANCER AND OCCUPATIONAL HEALTH. (E.) Hayes, R. L. (U.S.P.H.S., Dept. Health, Educat. Welf., Washington, D.C.). *J. Occup. Med.* 5(7):342-347, 1963.

It is recommended that routine examination of employees include a screening program for the early detection of oral cancer. Details for such a screening procedure which includes oral cytology for suspicious lesions are given. Supporting evidence for the desirability of such a screening program are the relatively high death rate (per 100,000) in males, 5.4 (3.4 for both sexes), the rapid increase in death rate and incidence rates with age (from 0.2-0.9 (for both) at 24-29 yr. to 20.5 and 64.3 death and incidence rates, resp., at 60-64). Moreover, recent data indicate that the 5 yr. cure rate rises from 30% for all tumors to 55% for tumors detected at less than 2 cm diameter, and that a

5 yr. cure rate of 90% may be obtained in tumors detected at less than 1 cm diameter.

- 63-987 FAMILIAL INHERITANCE OF TUMOR. (Jap.) Koga, N. (Dept. Surg., U. Kyushu Sch. Med., Fukuoka, Japan) and M. Mizoguchi. *Nippon Geka Gakkai Zasshi (J. Jap. Surg. Soc.)* 64(5):450-451, 1963.

In discussion of the case of a female (age 22) who died of carcinoma of the stomach, it was brought out that all members of the immediate family died of cancer except the father: a brother (age 19) of carcinoma of the rectum, a sister (age 22) of carcinoma of the pancreas, and the mother (age 48) of carcinoma of the stomach. Since a high incidence of malignant tumors are found in families with stomach cancer, diagnosis of the carcinoma is especially important.

- 63-988 CHANGES IN MORTALITY RATES FROM LEUKEMIA IN THE FIRST FIVE YEARS OF LIFE. (E.) Slocumb, J. C. (Dept. Epidemiol., Harvard Sch. Public Health, Boston, Mass.) and B. MacMahon. *New Eng. J. Med.* 268(17):922-925, 1963.

An analysis of data from the Vital Statistics of the United States and from Mortality Statistics covering leukemia deaths from 1933-1959 inclusive showed a steady decline in leukemia deaths in white children under 1 yr. of age starting at about 1940. Annual mortality (per million of population) in that age group has decreased from about 45 in 1940 to about 28 in 1959 (with a minimum of about 20 in 1956). Recently a second trend has been observed, consisting of a decreased mortality in white children under 2 and 3 yr. and by a corresponding increase in deaths among 3 and 4-year-old children. For nonwhites there is an indication that a decreasing trend may have started in children under 2 yr. in 1955-1959. The data allow several explanations. The observations suggest that search for newly introduced leukemogens affecting particularly white U.S. children 3-4 yr. of age may not be fruitful. If the observed decline in mortality is due to postponement of death, 2 features are noteworthy: the increase in survival must be considerable; and, at least for infants under 1 yr., and probably also the children 1-2 yr. old, it antedated any specific therapy known to increase survival of leukemic patients.

- 63-989 A KOREAN AUTOPSY MATERIAL. (E.) Ringsted, J. *Danish Med. Bull.* 10(3):90-96, 1963.

Autopsy findings are reviewed in 425 unselected cases (excluding stillborn babies and Caucasians) seen at the Scandinavian Teaching Hospital in Korea between 1958-1961. The frequency of malignant neoplasms was 21.4%, with an additional 1.2% of autopsies reporting benign or unspecified neoplasms. Distribution by site (autopsy series + a surgical series, giving 1042

malignancies evenly distributed between males and females) for the ten most common malignancies each sex is given. For males frequency was: stomach 18%; Hodgkin's disease, 8%, skin 8%; lung 7%; nose + ear + sinus 6%; larynx 4%; and leukemia, intestine, esophagus, and liver, each 3%. For females frequency was: cervix 11%; breast 11%; stomach 9%; intestine, thyroid, and Hodgkin's disease, each 4%; nose + ear + sinus and ovary + tubes, each 3%; and skin and choriocarcinoma, each 2%. Analysis of another published series as regards distribution by site for Korea, and comparison to data from the Danish Cancer Registry indicates that Koreans have a high incidence of stomach carcinoma, Hodgkin's disease, and liver tumors in both sexes, of cervix and choriocarcinomas in females, and of carcinoma of the penis in males. In contrast, the incidence of carcinomas of the testis, breast, testis, and prostate is lower than in Denmark. These data may be explained, in part, by a low life expectancy for Koreans. In the present series only 6.6% of deaths were over 50 yr., for all Korea the comparable figure was 10.0%, whereas for Denmark it was 82.3%. The high incidence of choriocarcinoma and primary cancer of the liver is said to be related to the high incidence of hydatidiform mole (the cause of which is not known) and of cirrhosis (50% in the autopsy series). In the present series about 50% of the patients with primary liver tumors had coexisting cirrhosis. Socioeconomic factors would appear to account for the high incidence of cancer of the cervix, and the low incidence of breast cancers. With regard to the latter, fibroadenomatosis was found only rarely in the biopsy material.

990 MALIGNANT DISEASES IN CHILDREN. (E.) Bennett, M. B. (Groote Schuur Hosp., Cape Town, S. Afr.). *Clin. Radiol.* 14(2): 165-170, 1963.

From data obtained in 159 tumors in children between 1952-1961 at the radiotherapy department of the Groote Schuur Hospital in Cape Town, the incidence of Wilms' tumor was about 20% (31/159), showing a greater incidence than seen in other countries. Most occurred in nonwhite children (20/31), which could not be a reflection of the overall sample (20/97 in whites and 11/62 in blacks). In contrast to studies from other areas, slightly more cases of Wilms' tumor were seen than neuroblastoma. In the present series, the latter was more frequent in white children (18/26) than in nonwhites (8/97).

991 REGIONAL VARIATIONS IN THE FREQUENCY OF BANTU OESOPHAGEAL CANCER CASES ADMITTED TO HOSPITALS IN SOUTH AFRICA. (E.) Oettlé, A. G. (Afr. Inst. Med. Res., Johannesburg). *S. Afr. J. Med.* 37(16):434-439, 1963.

Questionnaire to South African Hospitals re-

vealed differences in the relative frequency of cancer of the esophagus in Bantus, which varied more than 100 x between the regions of highest and lowest frequency. The crude figures show maximum frequencies (25.8 and 25.4/100 hospital beds/yr.) were in Transkei and Tembuland; the disease was also common in large cities, highest in Bloemfontein (12.6/100 beds/yr.), Johannesburg (6.5/100 beds/yr.) and 4 towns in the Cape province, Cape Town, Port Elizabeth, East London, and Kimberley (3.3-5.8/100 beds/yr.). The male:female ratio was always over 1.0 when determined, and was as high as 29 in one area. However, this is thought to be due in part to differences in social acceptance of hospitalization. Review of the data, of hospital records, and of literature indicates that the high incidence of esophageal cancer is of recent onset, and that the present data have only transient validity since increases have occurred in some areas during data collection. It was impossible to pinpoint the origin to urban or rural locations, and all available information indicates that the stimulus must be in both, and that distribution is patchy even within specific areas. In other parts of Africa regions of high incidence are Southern Rhodesia, Nyasaland, and Kenya and also at Khantorum in a nonnegro population. Review of mortality statistics suggests that among nonnegroes there is an increase among Asian females (possibly due to increased betel-chewing) and among Sudanese. Some provincial differences in mortality have been observed among South African whites.

63-992 REVIEW OF 110 CASES OF CANCER OF ORAL CAVITY IN PAPUA AND NEW GUINEA. (E.) Farago, C. (Radiother. Dept., Port Moresby Gen. Hosp., Papua). *Brit. Med. J.* 1:1264-1266, 1963.

On review of 110 indigenous Papuans and New Guineans receiving X-ray therapy for cancers of the oral cavity, no racial or geographical differences could be demonstrated, although a 1 pts., with the exception of 1 male and 1 female were inveterate betel nut chewers and the majority were tobacco smokers (twist tobacco rolled in newspaper or in tobacco leaves). The constituents of the betel nut and lime chewed by the majority of pts. were: fruit, leaf, root, or stem of Piper betle; Zingiber officinale; shell of Cocos nucifera; bread fruit Artocarpus incisa; and river shell lime. All tumors were squamous cell carcinomas, with a ratio of well differentiated: moderately differentiated: highly anaplastic of 4:2:1. The sex ratio was 3.2 males/1 female, probably due to social custom preventing women from attending hospitals. Age distribution was: 10-19, 2.7%; 20-29, 9.1%; 30-39, 29.1%; 40-49, 32.8%; 50-59, 23.6%; and 60-69, 2.7%. Distribution by site was: upper and lower lip 2.7%; tongue 27.3% (only 3/30 in females); floor of mouth, upper and lower gingiva, and hard palate, 1.8, 0.9 and 1.8%, resp., (all in males), and buccal mucosa, 65.5%.

- 63-993 MALIGNANT MELANOMAS IN FRENCH WEST AFRICA. (Fr.) Camain, R., A. Basset, Mensah, and I. Faye. *Bull. Soc. Franc. Derm. Syph.* 69(5):880-883, 1962.

A review of malignant melanomas seen at the Hospital Le Dantec showed 109 tumors: 105 in Negroes, 1 in a white Mauritanian, and 3 in white French subjects. Age ranged from 4-75 yr. with the majority aged 30-50 yr. There was slight predominance of women (37/50 in whom sex was recorded). The majority of melanomas were located in the foot (72/109 or 65%), with 68 located in the sole of the foot and 12 in the heel. The remainder were distributed as follows: eye 5; lower limb 3; head 2; thorax 2; fingers 2; and 1 each abdomen, breast and mouth. In 20/109 cases the tumors were metastatic to clinically occult primaries. Histologically the tumors consisted of proliferations of large polygonal cells, of pseudosarcomatous fusiform cells, or of both. Two typical histories are reported; 1 is of a woman, age 55, presenting with an ulcerated tumor 1 mo. after discovery of a pigmented "spot" in the heel; the other is of a boy, age 4, with a melanoma arising from a large congenital pigmented and pilary nevus in the dorsal region.

- 63-994 CANCER OF THE FEMALE GENITAL TRACT AMONGST THE SUDANESE. (E.) Lynch, J. B. (Faculty Med., U. Khartoum, Sudan), J. A. Verzin and A. M. Hassan. *J. Obstet. Gynaec. Brit. Comm.* 70(3):495-504, 1963.

Combined data from review of 1074 cancer biopsies in Sudanese women (Khartoum Civil and district hospitals, 1954-1961) showed the following cancer frequencies: breast 23.2%, cervix 15.7%, ovary 6.4%, corpus uteri 3.9%, chorion-epithelioma 2.0%, vulva 1.9%, vagina and fallopian tube <1% each, and other sites, 46.4%. Analysis of these frequencies shows that the distribution of cancers among Sudanese women is closer to that reported in Western countries than in some other African countries such as S. Africa, Uganda, the Congo and Portuguese East Africa. It is suggested that the low incidence of cervical cancer in the Sudan series may be due to circumcision in male Muslims. Age distribution was 24.3%, 28.6%, 22.9% and 17.1% at 30-39, 40-49, 50-59, and 60-69 yr. There was a high incidence of nulliparae among cervical cancer pts. (18.2%), but the frequency of nulliparae in a comparable control group (Oliphant, in Cardiff) was 15.6%.

- 63-995 SOME OBSERVATIONS ON THE EPIDEMIOLOGY OF BREAST CANCER AMONG MALES. (E.) Schottenfeld, D. (Dept. Prevent. Med., Cornell U. Med. Coll., Utica, N.Y.), A. M. Lilienfeld and H. Diamond. *Am. J. Public Health* 53(6):890-897, 1963.

Field study of 53 breast cancer (BR) pts., and of

53 colon cancer (CO) and 53 gynecomastia (GY) pts. matched by age and race, including 35 highly matched pts. (by age, race, hospital, and ward status) gave similar mean ages (65.1-65.7 yr.), marital status, religious distribution, and ratio of native to foreign born. However there was a trend toward a higher frequency of Jewish men in the highly matched group, 43% (CO, 31%; GY, 26%). BR had a slight but not significantly higher mean age at marriage, 29.1 yr. (approx. 26 yr. for CO and GY). The left:right breast ratio in cancer pts. was 1.14. Trauma to the breast was mentioned by 11.3% of BR pts., but by 5.7% GY and 3.8% of CO pts. Analysis of the occurrence of orchitis, orchiectomy, previous hormone therapy, family history of breast cancer, exposure to X-irradiation to chest, and antecedents of benign breast disease showed 22% of BR pts. with 1 or more characteristics, compared to 8% and 2% for GY and CO pts., resp. No differences could be detected among the 3 groups with regard to ABO blood groups, height/wt. relationship, diabetes, thyroid disease, liver disease, coronary heart disease, cancer of the prostate or neoplasms in general, and acne. Buccal smears from 25 breast cancer pts. showed the male chromosomal sex in all. (See also CRA 1(2):#338, 1963.)

- 63-996 CYTOLOGIC SURVEY FOR SQUAMOUS CANCER OF THE CERVIX IN HONOLULU, 1949-1962. (E.) Spencer, F. C. (Hawaiian Cancer Soc., Honolulu) and D. S. Yamamura. *Am. J. Obstet. Gynec.* 86(5):646-652, 1963.

Among 609 pts. with positive cytology out of a total of 160,696 examined between 1949-1962 for possible carcinoma of the cervix, three classifications were recognized. The number of cases with invasive carcinoma, carcinoma *in situ*, and dysplasia seen between 1949-1954 was, resp., 43, 28, and 7; between 1954-1959, 41, 94, and 26. In Hawaii uterine cancer deaths, 12.2/100,000 population were significantly lower than in the U.S. (16.1 in 1959). This difference was attributed to complete and extensive cytological technics. The authors conclude that the incidence of cervical carcinoma is independent of ethnic groups; large variations in incidence in certain areas would appear to be the result of poor methods of detection. In the discussion, L. A. Emge, stated that his experience in treating Japanese women, plus what he has read concerning Negro women, has caused him to conclude that ethnic differences do play a major role in the genesis of various types of carcinoma.

- 63-997 PREGNANCY AND LEUKEMIA. THE FUTURE OF OFFSPRING CONCEIVED DURING LEUKEMIA. (Ger.) Guash, J. *Folia Haemat. (Frankfurt)* 8(1-4):84-96, 1963.

On the basis of detailed histories of the offspring of 5 women who conceived and bore children following the diagnosis of leukemia, the author concludes that chronic myeloid leukemia in the mother has no significant effect on the fetus,

Since 3/3 children were healthy at the age of 17 yr. (including 2/3 born of mothers subjected to splenic irradiation during gestation), but that acute leukemia, treated or untreated, is likely to be fatal to the fetus (1/2 cases died with the mother and 1/2 was aborted). In an addendum, the author presents the family trees of men who fathered children during the course of chronic myeloid leukemia, 2 of whom were given splenic irradiation shortly before conception of their offspring; all the children, now adults, remain healthy. It is interesting, however, that the last 2 men (who were brothers), both presented with chronic myeloid leukemia at the age of 29 yr., 7 yr. apart.

998 CANCER IN LOWER NORMANDY. (Fr.)
Jacob, P., J. Robillard and J. S.
batucci. *Canad. J. Publ. Health* 54(6):43-66,
1963.

Cancers seen at the anticancer center of Caen (Lower Normandy) between 1952 and 1961 were reviewed and consisted of 1193 cancers in males, and 1377 in females. There was a geometrical increase in the number of new cases seen/yr., with a mean increase of 17%; this was greater in males (22%), than in females (12.5%). Comparison of tumor site frequency in the Lower Normandy series with another Normandy (Calvados) series, and one from Loir-et-Cher (typical of France) showed definite differences in the most common cancer sites. In males, for the Caen, Calvados, and Loir-et-Cher series, resp.: larynx 20.4, 7 and 6.2%; skin 15.6, 11.8, and 5.9%; esophagus 15.6, 14.8, and 8.7%; tongue 10.3, 4.0% and not stated; pharynx 7.1, 8.2% and not stated; lung 14, 12.5 and approx. 5.0%; prostate 1.5, 4.7 and 1.5%; and stomach 1.5, 10 and 21%. In women for the same three series, results were: uterus + cervix 41.2, 25.1 and 17.3%; breast 25.7, 24.9 and 21.7%; skin 16.3 and 7.4%; ovary + vagina + falva 7.0, 6.9 and 5.8%; rectum 3.2, 4.7 and 1.0%; urinary tract 1.0, 1.7 and 2.3%; stomach 8, 5.2 and 14.7%. Sex distribution remained approx. the same through all 3 series. In a discussion the author mentions continuing study of the role of foods in the various cancer site frequencies, with the aim of establishing a possible connection between the high frequency of esophageal cancer in Normandy males, and the drinking of Calvados (apple brandy).

999 CIGARETTE SMOKING AND CANCER OF THE LUNG.
IS THERE REALLY ANY ETIOLOGIC

RELATIONSHIP? (E.) Hyde, L. (VA Hosp., Long Beach, Calif.). *Cal. Med.* 98(6):313-317, 1963.

The author presents 28 points to demonstrate that the causal relationship of cigarette smoking to lung cancer is unproved. In 8 metropolitan countries the rate of incidence of lung cancer in whites was 105/100,000 males and in nonwhites, 112/100,000 males although the whites smoked twice as much. Mortality rates for lung cancer among urban dwellers were significantly higher than among rural groups, smoking habits notwithstanding. Immigrants (e.g. to New Zealand from Britain) were more susceptible to lung cancer than were natives. A good part of the increase in mortality from lung cancer may reflect population growth and improved diagnostic technic. Of 63 pts. with lung cancer, 65% had histories of long standing chronic bronchitis. Increasing incidence of lung cancer has been noted in countries where cigarette consumption has risen or remained static. The lower incidence of lung cancer in females is related to their earlier death due to cancer of the genitalia. Heavy smokers have not been shown to be stricken at an earlier age than nonsmokers. Air pollution and genotypic factors may be more genuine causes of lung cancer (29 references).

63-1000 SMOKING AND CANCER. RETROSPECTIVE
STUDIES AND EPIDEMIOLOGICAL EVALUATION.
(E.) Levin, M. L. (Roswell Park Mem. Inst., Buffalo, N.Y.). *J. Chron. Dis.* 16(5):375-381, 1963.

Among male pts. seen at Roswell Park Memorial Institute from 1945-1956 the incidence (percentage) of various types of cancer seen among 7145 non-smokers and 3016 cigarette smokers was, resp.: lung, 6.8 and 66.8; larynx 7.5 and 61.0; lip 14.4 and 45.5; buccal cavity, 10.3 and 48.0; pharynx, 12.5 and 53.9; bladder, 17.3 and 52.1; esophagus, 16.9 and 48.7. Total incidence was 25.7% (controls) and 39.2% (cigarette smokers). The relative risks for developing lung cancer when figures were adjusted for age and residence by smoking status were for cigarette smokers, 5.04; other smokers, 1.39; and nonsmokers, 1.00. When data were collected from a retrospective hospital study, the relative risks of male cigarette smokers for developing lung cancer was 6.3; cancer of mouth-pharynx-esophagus, 2.55 and bladder, 1.99; when data were collected from a prospective study of mortality data the risks for these same sites were 9.85; 2.18; and 1.93, resp. There is no available evidence that some characteristic other than smoking is responsible for this increased disease risk.

See also abstract no.: 801

MISCELLANEOUS

- 63-1001 CANCER: A UNIFIED DISEASE? (E.)
Nelson, D. H. (Roy. Victoria Hosp.,
Folkestone, Kent, England). Lancet 1:1112, 1963.

If it is postulated that aberrant malignant cells appear from the date of conception and their regulation is a normal event, all aspects on oncology form a unified picture of an immune mechanism with autoimmunity and anaplastic carcinogenesis at opposite extremes. The "cancer age" beginning in the 5th decade would be a manifestation of senility as an exhaustion of the natural immune mechanism. Tumors of the newborn would arise from implantation of mutant cells at an age too early for rejection. Double primary growths would be uncommon because the primary tumor would stimulate the response mechanism enough to reject a small new implantation but not enough to contain the established lesion. Appearance of another type of malignancy after complete extirpation of a primary growth would be expected.

- 63-1002 PROPERTIES OF A SOMATIC HYBRID BETWEEN MOUSE CELLS WITH DIFFERENT GENOTYPES. (E.) Gershon, D. (Weizmann Inst. Sci., Rehovoth, Israel) and L. Sachs. Nature (London) 198:912-913, 1963.

A new karyotype appeared in 1% of cells 26 days after initiating mixed passaging of strain L cells from s.c. tissue of a C3H mouse with polyoma-induced mammary tumor MT1 cells from an SWR mouse; and after 2-3 wk. the parent cell lines were eliminated. The modal chromosome number for the hybrid cells was 108, compared to L = 56 and MT1 = 68; the modal number of bi-armed chromosomes for the hybrid was 20, L = 21 and MT1 = 2. No such karyotype was found in control cultures passaged separately. No spontaneous polyoma virus (PV) production was detected in MT1 and hybrid cells; no PV was detected 36 hr. after PV infection with 10 PFU/cell in any of the 3 cell types. After transplantation of 10⁶ cells of hybrid, L or MT1 type to adult C3H, SWR or (C3H x SWR)F1 mice, at first there was growth in all groups but in some there was regression after 3-4 wk. Progressive growth was seen of L in C3H but not SWR, whereas MT1 grew in SWR but not in C3H; the hybrid grew only in F1 mice. When hybrid mice received PV (2 x 10⁷ PFU x 2, i.p.) 4 and 2 wk. prior to inoc. with hybrid or MT1 cells (5 x 10⁴ cells s.c.) tumors developed in 3/5 and 0/5, resp., compared to 4/5 and 5/5, resp., in nonimmunized controls, indicating that the polyoma-induced cell antigen may exist in the hybrid cell in a more weakly expressed form than in MT1 cells; or that the hybrid cells can better overcome the immune response of the host.

- 63-1003 STUDIES ON CERTAIN URINARY AND BLOOD SERUM ENZYMES IN BILHARZIASIS AND

THEIR POSSIBLE RELATION TO BLADDER CANCER IN EGYPT. (E.) Abul-Fadl, M. A. M. (Dept. Chem. Path., Cairo U., Egypt) and O. M. Metwalli. Brit. J. Cancer 17(1):137-141, 1963.

The av. total urinary β -glucuronidase excretion in 82 pts. with simple bilharziasis infections was 7,097 U/24 hr.; in 92 bilharziasis pts. with hepatosplenomegaly, 8460 U; in 102 bladder cancer pts. with definite bilharzial history, 15,588 U; and in 12 cases without such history, 14,950 U compared with 30 normal Egyptians, 3,742 U. The urinary alkaline phosphatase for these same groups were 2; 1.9; 4.9; and 3.8 U/100 ml, resp., compared with normals, 1.1 U. Urinary acid phosphatases were 31.7; 50.3; 17.7; and 6.1 U/100 ml, resp., compared with normals, 70.5 U. In pts. with simple bilharziasis, complicated bilharziasis and in those with bladder cancer with bilharzial history, the av. blood serum alkaline phosphatase (U/ml) was 10.1, 18.8, and 9.8, resp., compared with controls, 3.2; the av. blood serum glutamic-oxalacetic transaminase (SGO-T) was 12.8; 18.4; and 13.5 U/ml, resp., compared with normals, 10.6 the av. serum glutamic-pyruvic transaminase was 10.3; 18; and 11.8 U/ml, resp., compared with normals, 9.2. The latter 2 enzymes were somewhat influenced by stage and extent of liver involvement.

- 63-1004 ENHANCEMENT OF A SPONTANEOUS TUMOR IN THE STRAIN OF ORIGIN FOLLOWING VACCINATION WITH A TUMOR MEMBRANE FRACTION. (E., Abstract) Attla, M. A. (U. California, Berkeley). Proc. Am. Assn. Cancer Res. 4(1):3, 1963.

An emulsified cell membrane fraction (isolated by a simple overlaying technic with sucrose soln.) from homogenates of a spontaneous mammary carcinoma in an A/Crg1 female mouse, enhanced markedly the growth of tumor isografts in A/Crg1 female mice when admin. in complete Freund's adjuvant. Membrane fractions prepared from analogous normal tissue, or from tumor cytoplasmic fractions had no enhancing activity. The membranous nature of the active fraction was confirmed by phase contrast and electron microscopic examination.

- 63-1005 FORMATION OF TUMORS CONTAINING BONE AFTER I. M. INJECTION OF FL HUMAN AMNION CELLS INTO CORTISONE TREATED MICE. (E., Abstract) Anderson, H. C. (Sloan-Kettering Inst. Cancer Res., New York). Proc. Am. Assn. Cancer Res. 4(1):2, 1963.

Mice (15-18 g) treated with cortisone acetate (3 mg s.c.) at the time of inoc. with transformed human amnion cells (FL) i.m. in the right lower extremities developed tumor nodules separated from the host tissue by dense fibrous bands. In 12-day-old tumors cartilage and bone were present in irregular plaques, usually situated peripherally.

cells cultured *in vitro* have been shown stoichiometrically to contain more alkaline phosphatase than normal human amnion cells cultured under similar conditions.

63-1006 SOME PECULIARITIES OF METASTASIS FROM RAT SARCOMA SSR IMPLANTED UNDER THE SKIN OF THE TAIL. (Rus.) Maliugina, L. L. Inst. Oncol. Acad. Med. Sci. USSR, Moscow) and N. R. Miuller. Vop. Onkol. 9(6):56-59, 1963.

The rate of metastasis of rat sarcoma SSR in rats was determined after excision of the primary tumor by tail amputation 5-10 days after s.c. implantation. Rate of metastasis in intact male and female rats was 31% and 51%, resp., while operated rats rate was 63% and 69%, resp. The av. survival for intact groups was 16-19 days and 14-18 days for operated groups. Incidence of pulmonary metastases in intact and operated females was 32% and 31%, resp.; in males, 45% and 37%, resp. The corresponding incidence of lymph node metastasis in intact and operated females was 48% and 52%; in males 28% and 28%. The pulmonary metastases were solitary in 57% of the females and 55% of the males; the remainder were multiple. Removal of the primary tumor not only increased the rate of metastasis but stimulated tumor growth as well.

63-1007 TRANSFORMATION OF THE LIPOPIGMENTED RETICULOSIS OF PAUTRIER AND WORINGER INTO RETICULOSARCOMA. (Rus.) Likhachev, I. P. N. Burdenko Main Army Hosp., Moscow). Sov. Derm. Vener. 37(5):13-15, 1963.

Following a brief description of the principal characteristics of the Pautrier-Woringer syndrome (dermatosis accompanied by increased s.c. and later regional lymph nodes, plus brown pigmentation resulting from an accumulation of melanin and lipids in the reticular cells), the author presents a detailed case report on a 40-year-old man who developed ulcerative reticuloma of the leg after a 2.25 yr. history of symptoms despite treatment with ACTH and corticosteroids. A post-mortem histological study showed that the tumor cells retained the ability to accumulate fat and pigment (melanin and hemoderin). This case confirms the possibility of a transition between preblastomatous and neoplastic forms of reticulosis, and indicates that the Pautrier-Woringer syndrome should be considered a precancerous state.

63-1008 ANTITUMOR ISOIMMUNITY. (E.) Koldovsky, P. (Inst. Exp. Biol. Genetics, Czech. Acad. Sci., Prague). Acta Int. Cancr. 19(1-2):99-101, 1963.

A further report of work previously abstracted 1(4):#762 and #764, 1963, the author presents the following additional data. The percentage of Bp7/A and RBp7/A tumor cells killed

by reaction with isologous antiserum *in vitro* was 36% and 10%, resp. The number of survivors following inoc. of irradiated RBp7/A (4 mg) was 7/10 and Bp7/A (80 mg) 7/10. Small doses resulted in resistance while larger doses resulted in immunological paralysis.

63-1009 TRANSPLANTABILITY AND FUNCTION OF A THYROID AND PITUITARY TUMOR ARISING SPONTANEOUSLY IN AN HA/ICR SWISS MOUSE. (E., Abstract) Jacobs, B. B. (Roswell Park Mem. Inst., Buffalo, N. Y.). Proc. Am. Assn. Cancer Res. 4(1):31, 1963.

Routine autopsy of a 12½-month-old retired Swiss female revealed 2 adenocarcinomas, one in the thyroid and one in the pituitary, and also extensive breast development and adrenal hyperplasia. Both tumors grew progressively in about 50% of the first and second transfer hosts. The presence of the thyroid tumor was accompanied by splenomegaly, that of the pituitary tumor by decreased spleen wt., and increased adrenal and liver wt. In animals with both tumors, adrenal and liver changes were those characteristic of pituitary tumor hosts; spleens were not significantly changed. Presence of the pituitary tumor and/or the thyroid tumor was associated with decreased host pituitary wt. in females, but not in males.

63-1010 CHANGES IN MITOCHONDRIA AND THE ACTIVITY OF SOME REDOX ENZYMES DURING CARCINOGENESIS. HISTOCHEMICAL STUDIES. (Rus.) Raikhlín, N. T. Vop. Onkol. 9(4):113, 1963.

Histochemical studies of respiratory enzymes were made on 125 human malignant and 45 benign tumors, on normal tissues and during experimental carcinogenesis. The presence of all oxidation-reduction enzymes in cancerous tissues was established, but the activity of succinic and glycerophosphate dehydrogenases, TPN and DPN diaphorases and cytochrome oxidase was decreased, as compared with those of normal tissues. The activity of glucose-6-phosphate, 6-phosphogluconate, lactic and glutamic acid dehydrogenases was increased while the activity of malic and isocitric acid dehydrogenases was essentially unaltered. Mitochondria of cancer cells became more labile following any procedure that caused damage; there was an increase in their permeability to a series of substrates. Damage can be observed even in early stages, particularly in experimental carcinogenesis.

63-1011 CHROMOSOMES OF TWENTY CANCER EFFUSIONS: CORRELATION OF KARYOTYPIC, CLINICAL, AND PATHOLOGIC ASPECTS. (E.) Ishihara, T. (Roswell Park Mem. Inst., Buffalo, N. Y.), Y. Kikuchi and A. A. Sandberg. J. Nat. Cancer Inst. 30(6):1303-1361, 1963.

Detailed karyotypic analysis of 20 malignant

effusions was correlated with the clinical and pathologic data of the pts. studied. All effusions showed an abnormal modal number of chromosomes ranging from 39 to 133 with no specific number being more prevalent for any particular tumor. In 16 effusions "new" marker chromosomes were present whose origin could not be traced. Each effusion had a karyotype that differed from the others and was relatively stable. There was no correlation between the grade of malignancy of a tumor and the karyotypic findings: modal and chromosome numbers, presence or absence of markers. The potential significance of the genotypic changes will have to await the collection of more data.

- 63-1012 MALIGNANT TRANSFORMATION IN VITRO OF CELLS FROM C57BL MOUSE NORMAL PULMONARY TISSUE. (E.) Barski, G. (Gustave Roussy Inst., Villejuif (Seine), France) and R. Cassingena. J. Nat. Cancer Inst. 30(5):865-883, 1963.

Of 2 cell lines PG and PT established in vitro from a single explantation of normal lung tissue from a 2 mo. old female C57BL mouse, the PG line was transmitted by mechanical dispersion, the PT line by trypsinization. Within 6 mo. both fibroblast lines became adapted and transformed in vitro. PG cells at passages 15, 29 and 37, transplanted i.m. or s.c. to C57BL females or (C3H x C57BL)F₁ hybrids and in combination with 425 r total body X-irradiation did not produce tumors on periodic inoc. for 1 yr. PT cells at passage 16 produced sarcomas at the i.m. inoc. site in 2/4 in 2-4 mo.; these tumors were easily transplantable to C57BL but not to C3H mice. PT cells in passage 50, after i.m. inoc. into irradiated hybrid mice, produced sarcomas within 7 wk. which were easily transplantable to other hybrids and C57BL mice (giving 100% takes), but not to C3H mice. Secondary cell lines PT₂, PT₁, and PTT₁₂ were highly malignant fibrosarcomas which were histologically homogeneous. C3H mice receiving 10⁶ PT₁ or PTT₁₂ cells generally developed primary nodules which ceased to grow and regressed. Chromosomal analysis after 5 mo. in vitro growth of the PG and PT lines revealed predominance of hypotetraploidy and later presence of abnormal metacentric chromosomes. Morphologically PG and PT cells were fibroblasts with more typical and intermingling growth in PT cultures. The role of trypsin on PT cells may have been to interfere with the cell mitotic apparatus so as to increase the number of cell generations or to act as a selective factor.

- 63-1013 BLOOD-GROUP FREQUENCIES AND ASTROCYTOMA. (E.) Garcia, J. H. (Inst. Path., State U. New York, Brooklyn), H. Okazaki

and S. M. Aronson. J. Neurosurg. 20(5):397-399 1963.

Analysis of 630 consecutive pts. submitted to neurosurgery at Kings County Hospital Center, Brooklyn, N.Y., including 132 verified astrocytomas, 279 with other brain neoplasms, 124 with traumatic lesions, and 95 with miscellaneous disorders showed similar distributions of ABO blood types. Mean frequencies were: type O, 48.3% (47.0-51.6); type A 32.1% (30.6-34.1); type B 15.7% (13.7-16.9); and type AB, 4.0% (3.2-4.3). Mean frequencies for the astrocytomas alone were: 47.0%, 34.1%, 15.2% and 3.8%, resp

- 63-1014 METABOLISM OF TRYPTOPHAN IN CANCER OF VARIOUS SITES. (E.) Leppänen, V. V. (Dept. Med., Central Hosp., Kuopio, Finland) and M. Oka. Ann. Med. Exp. Fenn. 41(2):123-135, 1963.

Urinary tryptophan metabolites were studied in 10 cancer pts. (9 males; 8 pulmonary cancer, 1 breast, 1 esophageal cancer) and in 12 healthy controls (8 males). Half of the cancer pts. excreted an abnormal amount of kynurenine, anthranilic acid, 3-hydroxyanthranilic acid, xanthurenic acid and/or 5-hydroxyindoleacetic acid before and/or after a loading dose of L-tryptophan (2 g). Before and after tryptophan loading, the total amount of urinary kynurenine, anthranilic acid, 3-hydroxyanthranilic acid and xanthurenic acid was 2x higher in cancer pts. than in controls. After tryptophan loading the excretion of 3-hydroxyanthranilic acid and 5-hydroxyindoleacetic acid was significantly increased.

- 63-1015 AETIOLOGY OF LEUKAEMIAS. (E.) Schöyer, N. H. D. (Gorinchem, The Netherlands). Lancet 1:1427, 1963.

In a letter to the editor the report of Tough et al. indicating that 2/25 cases of chronic myeloid leukemia were Ph¹-negative is analyzed. The present author is concerned by the implications of the Edinburgh group that chronic myeloid leukemia is a conglomerate of subgroups including a Ph¹-negative, and an X 0 Ph¹-positive subgroup. It is suggested that the subgroups may be stages in the development of the disease. Tough et al. stated that all of 253 Ph¹-negative cells (of 1420 examined) belonged either to rare cases where the Ph¹ chromosome is not found (all with an unusually long history after diagnosis) or to pts. with marrow insufficiency developed during or after treatment. The present author suggests that perhaps the Ph¹-positive subgroup could be a late stage of the disease. He is uncertain of the significance of combinations with X 0 cell lines in the etiology of leukemias. (See also 1(5):#784, 1963.)

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National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE Public Health Service

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration(s)	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health, USA
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit(s)
e.g.	for example	ppm	parts per million
FFU	focus forming unit(s)	pt. (s)	patient(s)
g	gram(s)	RBC	red blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
ID ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution(s)
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit(s)
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose(s)	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	ln.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	lt.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukranian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

63-1016 POSSIBLE INTEGRATION OF VIRAL NUCLEIC ACID INTO THE GENOME OF ANIMAL CELLS.

(E.) Kohn, A. (Israel Inst. Biol. Res., Ness-Ziona). Pp. 169-218 in Progress in Medical Virology, Vol. 5. Berger, E. and J. L. Melnick (Eds.). 29 Figs. and 10 Tables. Hafner Publishing Co., Inc., New York, 1963.

After a discussion of virus-cell interaction in bacteria, including a full description of lysogeny, lysogenic conversion, and methods of induction of lysogeny, the author compares bacterial and animal cells in their relation to viruses. In a discussion of virus-animal cell interaction, 2 types are detailed: the carrier latent state (few cells support the virus) and the occult state (viral genome divides synchronously with host genome). Various systems leading to the carrier state are described; immune tolerance is considered an example of the carrier state at the whole organism level. Among lysogeny-like states in animal cell populations in vivo the author includes the rabbit papilloma, rat fibroma, and avian viruses such as fowl pox. Among studies of virogeny in vivo, the role of nucleic acids (without detectable antibody formation) is discussed for leukemias, lymphomas, and other persisting viral agents such as serum hepatitis, swine influenza and hog cholera. Studies of virogeny in animal cells and cell clones in vitro have shown a number of mechanisms: neoplastic conversion of myeloblasts, followed by differentiation in chicken myeloblastosis; neoplastic conversion and immunity observed in polyoma infection and neoplastic conversion and induction found in Rous sarcoma infection. The author concludes by summarizing recent studies where viral integration into host cell genome has been found, including Rous sarcoma, polyoma, polyhedrosis, and papilloma viruses. In a few instances where a proviral state has not been demonstrated (Sigma virus, avian myeloblastosis virus, simian virus 40), further investigations are warranted. (Approx. 210 references)

63-1017 PRELEUKEMIC STATES. (Ger.)

Fleischhacker, H. (Hanusch Hosp., Vienna). Arch. Haemat. (Frankfurt) 8(1-4):3-9, 1963.

Review of the case histories and autopsy findings in 115 pts. with acute myeloblastic leukemia showed that 89 cases were definite myeloblastic leukemias from the outset, 21 first presented as panmyelopathy, 1 as osteomyelofibrosis, 2 as reticulosis and 2 as refractory myeloblastic anemia. Most of the pts. were over 50 yr. of age, and 69% were admitted in the spring or fall. Among 3 cases reported in detail, the 1st had a history of reticulosis treated by X-ray; the 2nd had worked for 4 yr. with lead, zinc and aromatic hydrocarbons, as well as ingesting large quantities of headache tablets, before developing a panmyelopathy; the 3rd had worked

with radium for over 10 yr. before a marked gradual decrease in RBC and WBC was noted which eventually developed into acute leukemia. On the basis of his personal experience, the author divides granulopoiesis into resting, proliferative and reserve elements, and suggests that all conditions involving prolonged damage to the proliferative elements should be looked upon as preleukemic states. It is also quite likely that the initial heritable mutation leading to the increasing enzymatic deficiency and cellular proliferation characteristic of chronic myeloid leukemia is due to a virus, which may, however, remain latent. Carcinogens and other nonspecific stimuli may produce frank leukemia by stimulating the synthesis of masked viruses. As the chronic leukemic condition, or other conditions such as osteomyelosclerosis or polycythemia, develops, the marrow cells become increasingly immature, leading to the eventual crisis of stem cell proliferation, which may also be hastened by excessive treatment with radiation or cytostatic agents. (No references)

63-1018 VIRUSES AND CANCER. (E.) Horsfall, F. L., Jr. (Sloan-Kettering Inst. Cancer Res., New York). Acta Un. Int. Cancr. 19(1-2):247-249, 1963.

The author reviews the properties of various carcinogenic viruses and states that these viruses are comparable to the other members of the family of viruses. The controlling role of the host's genome in the viral induction of cancer is emphasized. (19 references)

63-1019 AIR POLLUTION AND LUNG CANCER. (E.) Lawther, P. J. (St. Bartholomew's Hosp. Med. Coll., London). Practitioner 190:720-725, 1963.

The results of several recent studies dealing with the possible existence of an "urban factor" contributing to the frequency of lung cancer in smokers are discussed briefly. A possible solution of conflicting results would be the establishment of a subtle sensitivity in British people to the combined effect of cigarette smoking and air pollution. (21 references)

63-1020 INVESTIGATION INTO CIGARETTE SMOKING AND ATMOSPHERIC POLLUTION IN THE AETIOLOGY OF LUNG CANCER. (E.) Doll, R. (University Coll. Sch. Med., London). Meth. Inform. Med. 2(1):13-19, 1963.

A review of numerous statistical studies confirms the relationship between cigarette smoking and cancer of the lung. The evidence has been consistent in both retrospective and prospective studies. A causal hypothesis for cigarette

smoking and cancer is not established, but is supported by study of pathological changes in the bronchial mucosa of smokers and nonsmokers, and by results of animal experiments. While it is clear that atmospheric pollution has little effect on lung cancer incidence in nonsmokers, there is strong statistical evidence that lung cancer mortality in smokers is much higher in large cities than in rural areas. (34 references)

63-1021 RADIATION CARCINOGENESIS. (E.) Court Brown, W. M. (Radiat. Res. Unit, Western Gen. Hosp., Edinburgh, Scotland). *Practitioner* 190:715-719, 1963.

The authors note that studies done on survivors of the atomic bombings during World War II plus follow-up work on those that received thymus irradiation during childhood and antenatal irradiation for diagnostic procedures, have all tended to confirm a positive correlation between irradiation and carcinogenesis. However, in all these instances relatively large doses are or have been involved. Thus, the best we can do at present is to extrapolate from curves of known, larger damaging doses in order to determine accurately whether or not low doses of irradiation are carcinogenic. (No references)

63-1022 IMMUNO-MORPHOLOGICAL IMPLICATIONS IN THE MECHANISM OF CARCINOGENESIS. (E.) Cajano, A. (Tumor Inst., Pascale Found., Naples, Italy). *Acta Un. Int. Cancr.* 19(1-2):213-215, 1963.

Carcinogenesis is discussed as a possible "incompatibility disease" due to cellular or subcellular auto-antibodies. Analogies are drawn between cancer and findings in animals inj. with heteroimmune sera against cells or organs, and the conclusion is drawn that the pathogenesis of cancer is a problem in immunopathology. Six fundamental points are discussed in detail. (1) Auto-immunization or the increase in immunologic auto-incompatibility or of an incompatibility due to auto-antibodies after involvement of "immunologically competent" cells. (2) Relationships between mesenchyme and parenchyme, and the concept of physiologic auto-incompatibility. (3) Classification of tissue cells into labile, stable and fixed, with either intermitotic or post-mitotic cells. (4) Auto-antibodies and target structures against which 2 types of effects are possible: cytotoxic, leading to necrosis and destruction; and cytostimulating, leading to mitotic stimulation and atypical mitoses. (5) Relationships between cytoplasm and nucleus, which follow a pattern similar to that observed in microbial genetics. (6) Mode of action of auto-antibodies, where neoplastic proliferation is considered as due to contact with auto-antibodies of the structures concerned with mitosis, or of cell structures indirectly related to mitosis, leading to

proliferation similar to that observed in the "immunologically competent" cells after contact with hetero-antigen. (19 references)

63-1023 CARCINOGENIC AND LEUKEMOGENIC ACTIVITIES OF IONIZING RADIATIONS. (It., Abstracts) Vallebona, A. (Radiol. Inst., U. Genoa, Italy). *Minerva Med.* 54(38):1411-1412, 1963.

Theoretical and practical aspects of oncogenesis by irradiation are reviewed very briefly. Although irradiation produces a broad spectrum of tumors, connective tissue neoplasms appear to have a shorter latent period than epithelial neoplasms. The author points out that experimental irradiation-induced leukemias appear to show different requirements for various animal species, physical factors (modality, dose, type of irradiation), and biologic factors (age, sex, effect on some organs, virus infections). Furthermore some "protective" compounds (unspecified) have an inhibitory or retarding effect on the growth of most radiation-induced tumors but stimulate the appearance of lymphoid tumors and of leukemias. (No references)

63-1024 GENETIC ASPECTS OF DYSPROTEINEMIAS. (Fr.) Jerome, H. (Inst. Hyg. Child. Dis., Paris). *Ann. Biol. Clin.* 2(1-2):135-145, 1963.

After a brief discussion of mechanisms of gene action the author reviews some cytogenetic changes known to be associated with abnormal protein synthesis. In Waldenstrom macroglobulinemia recent reports have established the presence of 47 chromosomes, 1 larger than pair #1 in about 50% of the cells examined. This evidence together with the presence of a $\beta 2$ band on electrophoresis and of a $\beta 2$ -M protein on immunoelectrophoresis of plasma from the asymptomatic mother of 2 male pts. is taken as suggestive of trisomy inheritance. In these cases a precocious translocation of a small chromosomal fragment could result in progeny of 2 types, trisomics (disease) and monosomics (lethal), with a position effect evidenced in the mother. In other cases somatic mutations could either set off, or cause directly, the abnormal protein synthesis. In myelomas cytogenetic studies have shown a variety of abnormalities, the most consistent is a chromosome count of 45 in over 50% of the cells, with absence of an acentric strand, either #21, 22 or 4. Other pts., however, have supernumerary chromosomes. No familial involvement has so far been reported. In chronic myeloid leukemias deletion of the long arm of one of the #21 pair has been correlated with a decrease in the alkaline phosphatase activity of granulocytes, whereas in mongoloids with trisomic #21, the alkaline phosphatase activity is increased 1.5x that of normal granulocytes. (26 references)

- 025 FRIEND'S DISEASE. (Fr.) Latarjet, R. (Radium Inst., Paris). Bull. Assn. C. Cancer 49(4):345-350, 1962.

history and macroscopic and microscopic changes of Friend's leukemia are reviewed briefly. Described are physical, biological and immunologic characteristics of the virus. The state of the virus in tumor-bearing vaccinated animals is unclear, and the nature of the viral nucleic acid is still unknown, although suspected to be RNA. Other unexplained effects of the virus include the ability to induce varied types of differentiation, such as formation of osseous lesions in diseased spleens. (9 references)

- 026 INACTIVATION OF FRIEND'S VIRUS BY ULTRAVIOLET AND X-RAYS. (Fr.) Latarjet, R. (Radium Inst., Paris) and L. Chamaillard. Bull. Assoc. Franc. Cancer 49(4):382-389, 1962.

Survivants from homogenates of spleens of Swiss mice with Friend's leukemia were irradiated and tested for viability of the virus by i.p. injection of various dilutions into Swiss mice for 14 days. The calculated incident X-ray doses required to produce a decrease in pathogenic activity of 90% and 99% were 400 and 800 kr, resp. For the dose required for a 90% decrease was approximately 10,000 ergs/mm². In a typical experiment in 1 extract of initially low viral activity (1/10 dil., latency 115 days) UV irradiation frequency of leukemias was decreased to 5/5, and latency was decreased to 5/5. Another extract irradiated with 2500 ergs failed to cause leukemias in 6 animals, after UV irradiation with 25000 ergs, leukemias were induced in 4/10. Comparison of these results and of known doses required to inactivate the Friend's leukemia virus suggest that the oncogenicity of the Friend's leukemia virus resides in a RNA fragment of less than 3500 nucleotides.

- 027 COMPARISON OF THE SYMPTOMATOLOGY OF HUMAN AND ANIMAL LEUKEMIA, IDENTICAL DIFFERENT SYMPTOMS. (Ger.) Otto, H. (Disch. Hosp., Kothlen (Anhalt), Germany). Zschr. L. Fortbild. (Berlin) 57(8):461-465, 1963.

After comparing human and animal forms of leukemia from the following points of view: etiology, morphology, mode of propagation (infectiousness), clinical course, and general chemotherapy. The etiology of various forms of animal leukemia is documented and the evidence pointing to a similar etiology for human leukemia is discussed. It was mentioned that statistics in West Germany show that incidence of human leukemia has increased since 1948. It occurs most often between ages of 1-10 and after 50. (32 references)

- 028 BLOOD GROUPS AND LEUKEMIA. (Ger.) Gold, E. R. (Southwest Reg. Transf. Ctr., London, England) and L. Holländer. Blut (München) 88-193, 1963.

A survey of literature reports of abnormal blood group findings in cases of leukemia reveals that most of them concern the ABO system, and specifically the A-antigen. So far, changes in the ABO, Rh- and MNSS-systems were observed. These changes range from quantitative modification of agglutination to radical qualitative changes of the antigen type. Further, these changes can involve one or several blood group systems. In cases in which only one system is involved, either one or both antigens can be changed. When only one system and one antigen of this system is involved, all of the cells can be changed equally, or only a portion of them. Most of the cases were found in male pts. These changes are compared with those found in variants of blood group antigens occurring in normal subjects and with the changes produced in RBC by chemotherapeutic agents. The possibility and the nature of a somatic mutation as the cause of the antigenic changes are discussed. (41 references)

- 63-1029 NORMAL GROWTH AND CANCER. (E.) Medes, G. (Inst. Cancer Res., Philadelphia, Pa.) and S. P. Reimann. J. B. Lippincott Co., Philadelphia, 268 pp., 1963.

A review of some aspects of cancer research, including a brief account of the physiology of the cell and cytogenetics and, in more detail, carcinogenesis. The book is intended for scientists, physicians and others who are broadly acquainted with the basic sciences but not specialists in cancer research. It is, as the authors point out, a history of progress in the study of cancer, with many excursions into related fields, and has extensive bibliographies, and includes a separate bibliographic index.

- 63-1030 THE ROLE OF TISSUE CULTURES IN THE STUDY OF THE PROBLEM "VIRUSES IN ONCOLOGY." (E.) Timofeevsky, A. D. Acta. Un. Int. Cancr. 19(1-2):230-233, 1963.

In a brief review of the results of the search for a viral etiological agent in malignant human tumors, the author states that in tissue cultures infected with human tumor extracts, an oncogenic effect might be produced by virus arising spontaneously in the tissues. Also mentioned is the disproportion found between the comparatively short period and high rate of reproduction of polyoma virus (strain 2510-6B) on the one hand and the slow progress of the cytopathogenic effect on the other. This has led to the suggestion that the viral population of this strain was heterogeneous and composed of inhibitor-susceptible and inhibitor-nonsusceptible particles. (13 references)

- 63-1031 PAPILLOMAS AND CANCER: ARE VIRUSES THE CAUSE? (E.) Rapp, F. (Texas Med. Ctr., Houston). New York J. Med. 63(12):1786-1790, 1963.

The relationship of viruses to human and animal

papillomas is discussed, with special emphasis on the unexplained disappearance of the virus in experimental animals during transformation of papilloma to carcinoma. Recent findings suggesting that incomplete viruses may be detectable on electron microscopic study of appropriately treated preparations are mentioned. (53 references)

- 63-1032 STEROIDS AND CANCER. (E.) Kelly, M. (Inst. Rheumatology, Melbourne, Australia). Lancet 1:1375-1376, 1963.

In a brief review of the use of steroids given prior to or in conjunction with the development of cancer, the author states that while positive proof that steroids promote cancerous growth is still lacking, much clinical and experimental evidence is at least highly suggestive. (17 references)

- 63-1033 PRECANCEROUS AND PSEUDOCANCEROUS DERMATOLOGIC DISORDERS. (Ger.) Fischer, H. (Clin. Derm., Eberhard-Karls-U., Tübingen, Germany). Med. Klin. 58(27):1097-1101, 1963.

In a general review are discussed precancerous conditions, their causes (including physical stimuli, exogenous and endogenous factors) and their latent periods. The author concludes that dermatologic disorders can become precancerous only when they induce atrophy (rather than hyperplasia) of the prickle cell layer and/or of connective tissue; although these changes must also be followed by long continued or repeated exposure to some (nonspecific) stimulus capable of inducing regenerative epithelial proliferation in the affected area. (37 references)

- 63-1034 THE PROBLEM OF CANCER. (Ger.) Bauer, K.-H. (Clin. Surg., U. Heidelberg, Germany). Springer-Verlag OHG, Berlin-Göttingen-Heidelberg. 2nd. ed. 1099 pp., 1963.

An extensive review of the whole field of cancer diagnosis, treatment, prognosis and prophylaxis includes sections on carcinogens and carcinogenesis. Occupational carcinogenesis, classification of cancers developing from specific precancerous lesions, and statistics on incidence in humans and animals are discussed. An interesting fact is pointed out, i.e.; that although mesenchymal tissue contributes to 82.5% of the body

and epithelial tissue to 17.5%, general incidence of sarcoma is only 8%, and of carcinoma 92%. There is no convincing evidence that cancers are hereditary disorders or disorders involving a hereditary predisposition, with the exception of a few, rare, hereditary abnormalities which may predispose to development of secondary cancers (e.g., xeroderma pigmentosum, polyposis testini, neuroblastoma retinae). The role of infections in carcinogenesis is discussed at length including the alleged possibility of a general viral etiology (which the author believes to be without objective support, except in the case of a few specific tumors). Except for smegma as a causal factor in cancers of the penis, he says no naturally arising, endogenous carcinogen has yet been demonstrated *in vivo*; and that of approximately 600 known exogenous carcinogens (most of which are reviewed in detail), all are products which man himself has developed as by-products of civilization which are essentially foreign to the human body. He concludes that, whatever the specific carcinogen or combination of carcinogens involved, the resulting cancer cell is a variant of the cell of origin which involves a somatic mutation propagated through succeeding cell generations to modify the growth regulatory mechanism with increasing age of the affected cell group paralleled by an increasing degree of cell mutability in a fashion entirely consonant with deVries' theories of biological mutation and with Planck's quantum theory. He also concludes that this mutagenic etiology of cancer, in response to repeated or continual exposure to the type of exogenous carcinogens described above, is sufficiently firmly established (i.e., "irreparable, irrevocable, and irreversible") to indicate that the eventual solution to the problem will lie in prophylactic removal of such carcinogens from the environment rather than in the development of any chemotherapeutic or other type of "cure". (Extensive bibliography)

- 63-1035 PATHOLOGY OF GRANULOPOIESIS. (Ger.) Begemann, H. (1st. Dept. Med., City Hosp., Munich-Schwabing, Germany). Deut. Med. 5(11):314-319, 1963.

A review of the pathogenesis of acute and chronic myeloid leukemias, their increasing incidence and mortality, and their etiology; including exogenous influences (radiation, chemical agents and infections) and endogenous factors (familial chromosomal), followed by a discussion of the non-leukemic diseases, allergic agranulocytosis and toxic granulocytopenia (both largely drug-induced) (86 references)

See also abstract nos.: 1086, 1210

PHYSICAL CARCINOGENESIS

36 MICROTUMOURS OF BONE PRODUCED BY RADIOACTIVE STRONTIUM IN RATS.

(Abstract) Skoryna, S. C. (Dept. Exp. Path., McGill U., Montreal, Canada), T. M. D. R. Webster, and D. S. Kahn. Proc. Am. Cancer Res. 4(1):63, 1963.

Inj. with Sr^{89} (0.1-4.5 μ C/g singly or in ed doses) were sacrificed at intervals up yr. after treatment. The earliest changes outable to the isotope were marrow fibrosis icroscopic collections of small cells with chromatic nuclei, found in vertebrae and etaphyses of long bones, in relation to the hyseal growth apparatus. These "micro-s" had histologic characteristics com-e with malignancy. In some instances r collections of the same type were found ing cortical bone and replacing normal w structures. Some "microtumors" were after up to 24 mo. which had not become ive.

37 STUDY ON OCCUPATIONAL LUNG CARCINOMA.

(6th REP.) INDUCTION OF TUMOR TO T-PNEUMOCONIOSIS BY ACETYLAMINOFLUORENE. (Abstract) Takemoto, K. (Dept. Hyg., Sch. Med. Dent.), M. Toda, K. Namie and hima. Nippon Eiseigaku Zasshi (Jap. J. 18(1):140, 1963.

tos (20 mg. of 30-200 μ fragments) was inj. tracheally into female rats weighing 100 g; 4 wk. (when the inflammatory reactions had ded) acetylaminofluorene, 5 mg/day, was in the diet for 6 wk. The minimum carci-c dose was 500 mg. The relative incidence enocarcinoma to epidermoid carcinoma in ols was 5:1; in rats previously treated with os, there was a higher incidence of epi-d carcinoma. The fact that more epidermoid omas occurred around areas of fibrosis due e asbestos suggests that asbestos plays ole in carcinogenesis.

38 EFFECTS OF X-IRRADIATION ON PULMONARY ONCOGENESIS INDUCED BY URETHAN IN THE (Fr.) Duplan, J.-F. (Pasteur Lab., a Inst., Paris). Bull. Ass. Franc. Cancer 260-269, 1962.

and female XVII mice receiving urethan (U; 50 0 g 2 x/wk. x 10 i.p.) showed an uneven rate g wt. gain, more rapid for the right lung or the left lung; lung tumors also appeared r in the right lung (per mouse, 15 at 95, 205-300 days) than in the left (6/mouse at /mouse at 205-300 days). X-irradiation of orax (1200 r 2-3 days before U treatment 0 r x 2 at 1 wk. intervals 3-4 days before

U treatment) decreased the rate of formation and number of tumors (per mouse) in both lungs to 2 and 5 for the right, and 16 and 22 for the left lung at the 2 X-ray dosages, resp. At the lower X-ray dose there was an early increase in lung wt., possibly because of an antiinflammatory effect of U. X-irradiated controls showed a marked early rise in lung wt., followed by a re-turn to normal, but no tumors in the 300 days of observation.

63-1039 DEVELOPMENT OF LEUKEMIA IN LETHALLY IRRADIATED MICE PROTECTED WITH CELLS FROM MICE OF A HIGH INCIDENCE LEUKEMIA STRAIN.

(E., Abstract) Hays, E. F. (Dept. Biophys. Nucl. Med., UCLA Med. Ctr., Los Angeles, Cal.) and E. White. Proc. Am. Assn. Cancer Res. 4(1):27, 1963.

Protection of C3H mice with C3H bone marrow cells after lethal irradiation (750-800 r) allowed survival of 22/22 animals. Protection of C3H mice with bone marrow cells from the high leu-kemia strain AKR/JAX resulted in bilateral paro-tid and adrenal tumors in 1/21 mice at 24 wk. after irradiation. Typical thymic leukemia de-veloped in 1/28 irradiated C3H mice which re-ceived bone marrow and thymic cells from AKR mice. Cells from the enlarged organs of this animal produced leukemia in AKR, but not in C3H mice. Median survival of AKR skin grafts was 21 days in animals protected with C3H cells, but 45 days in animals which received AKR cells. Results suggest that lethally irradiated mice protected with AKR bone marrow cells become tolerant to AKR tissues. Consequently the AKR bone marrow and thymus cells remain viable in the homologous host, and eventually express their leukemic potentialities.

63-1040 CHROMOSOMAL ANOMALIES FOLLOWING TOTAL IRRADIATION IN MAN. (Fr.) Papiernik-Berkkauer, M. (St. Louis Hosp., Paris), J.-L. Amiel and G. Mathé. C.R. Acad. Sci. (Paris) 256(24):5232-5235, 1963.

A 6-year-old pt. with acute lymphoblastic leu-kemia received total body irradiation with Cobalt 60 (800 r) during a period of apparent complete remission. Chromosomal preparations of leukocytes prepared after addition of phytohemagglutinin 42 days after irradiation and 20 days after isogenic bone marrow transfusion revealed abnormalities consisting of all the unstable types, as well as two particular chromosomal rearrangements. One consisted of a large telocentric chromosome of a size larger than that of group 13-15, found in 8 cells out of 72; the other was a sub-telocentric chromosome whose size was always larger than that of group 4-5, and was found in 15 cells out of 72 examined. These abnormalities were found to occur simultaneously in 2 cells.

- 63-1041 THOROTRAST TUMORS OF THE LIVER.
(Ger., Abstract) Lembcke and Möbius.
Zbl. Allg. Path. 104(5-6):312-313, 1963.

The authors report 3 cases of malignant hepatic tumors occurring 19, 29 and 32 yr. following the use of Thorotrast for diagnostic purposes. All 3 cases had liver cirrhosis and in 2 of them, tumors of the vessels of the liver were present, as was the case in 13 of the 21 cases of Thorotrast tumors recorded in the literature.

- 63-1042 MALIGNANT TRANSFORMATION OF BENIGN LARYNGEAL PAPILLOMAS IN CHILDREN AFTER RADIATION THERAPY. (E.) Majoros, M., K. D. Devine and E. M. Parkhill. *Surg. Clin. N. Am.* 43(4):1049-1061, 1963.

Microscopically proved papilloma of the larynx was seen in 101 children at the Mayo Clinic during a 47-year period (1914-1960). Squamous cell epitheliomas developed subsequently in six (14%) of the 43 pts. who received irradiation (radium and/or X-ray) therapy during the course of their disease. This did not occur in any of the 58 cases which had received no irradiation. The 6 pts. received radiation treatments for 2-8 yr.; 6-21 yr. elapsed between the beginning of radiation therapy and development of malignant change.

- 63-1043 SCAR CANCER IN THE ATOMIC BOMB SURVIVORS. (E.) Tezuka, H. (1st Dept. Surg., Nagasaki U. Sch. Med., Japan), C. Harano and R. Shirabe. *Acta Med. Nagasaki* 7(1-2): 7-15, 1963.

Two cases of squamous cell carcinoma occurring in scars from burns from the A-bomb explosion in Nagasaki are reported. The first in a man, age 50, appeared after 4 mo. on the back of the left hand; the other was found in a woman, age 54, on the left leg, first noticed 4 mo. after exposure, but she sought treatment after 10 yr. The pts. were 1300 and 2400 m from the hypocenter, resp., and both suffered acute radiation sickness. Four other reported cases of skin cancer in A-bomb survivors at Hiroshima are reviewed and findings are compared to those in other burn cancers.

- 63-1044 DEPENDENCE OF FREQUENCY OF X-RAY-INDUCED CHROMOSOME ABERRATIONS ON DOSE

- RATE IN THE CHINESE HAMSTER. (E.) Brewen, J. (Dept. Biol., Oak Ridge Natl. Lab., Tenn.). *Proc. Nat. Acad. Sci. USA* 50(2):322-329, 1963.

After X-irradiation of the cornea of Chinese hamsters a dose rate related effect was observed on the frequency of chromosome aberrations scored on metaphases obtained at 6 hr. after irradiation (0.3 ml 1% colchicine i.p. at 1 hr. before sacrifice). The effect was similar on chromatid deletions and chromatid exchanges averaging 1.04×10^{-3} breaks/cell/r at 2 r/min compared to 1.94×10^{-3} at 60 r/min., and 2.95×10^{-3} at 600 r/min. in corneas treated with a dose of 50 or 100 r. The dose rate related effect was not observed when corneas were irrigated with puromycin (100 μ g/ml) throughout the period of irradiation, in which case the frequency of breaks from 50 r was the same at all 3 dose rates, $3.12-3.52 \times 10^{-3}$ breaks/cell. Results suggest that the dose rate related effect is due to inhibition of rejoining, since rejoining requires protein synthesis (inhibited by puromycin). In all cases evidence of rejoining was obtained as decreased frequency of breakages in metaphases examined 12 hr. after irradiation. The breakage rate/cell in untreated, unirradiated controls was 0.006, compared to 0.007 in saline irrigated corneas, and 0.014 in corneas of puromycin-treated nonirradiated controls.

- 63-1045 NEOPLASTIC PLASMA CELL. (E.) Berlin, N. I. (NCI, Bethesda), R. Merwin, M. Potter, J. L. Fahey, P. P. Carbone and M. J. Cline. *Ann. Intern. Med.* 58(6):1017-1036, 1963.

In mice, plasma cell tumors were found to be induced by millipore membranes (3/36), acryloid discs (1/19), Lucite discs (2/9) and Lucite borings (5/12) when placed i.p. in mice (in the absence of any inoculum). Lucite rings or fibers were ineffective. At present, no explanation of this is known. Sarcomas were also induced by the discs but not by the rings and fibers. In mice 2-ring chambers of large diameter (18 mm) induced plasma cell tumors in 3/26; with 1 ring chambers 13 mm in diameter, none resulted in 26. With inclusion of C3H mammary tumor with agent in the chambers, results were 11/54 and 0/25. It was found that although plasma cell tumor protein secretion may vary from animal to animal, the type of protein secreted remains constant in any one tumor and can subsequently be passed from one animal to another without change.

See also abstract nos.: 1021, 1083, 1092, 1101, 1109, 1118, 1129, 1163

CHEMICAL CARCINOGENESIS

046 THE APPEARANCE OF LATE TUMORS IN DOGS INJECTED WITH CHEMICAL CARCINOGENIC AGENTS. (Rus.) Krotkina, N. A. (Inst. Med. Acad. Med. Sci. USSR, Moscow) and M. A. Masova. Vop. Onkol. 9(7):15-21, 1963.

Osseous inj. of carcinogen to rabbits and dogs produced changes in the bone and often distant organs, especially in the endometrium of the female. 9,10-Dimethyl-1,2-benzanthracene (DMBA; 8-13 mg) inj. into female dogs produced proliferative changes in the endometrium which often had characteristics of malignant tumors with extensive metastases into internal organs. Distant tumors frequently appeared without the development of malignant tumors at the site of admin. Tumors usually appeared 1.5-2 yr. after inj. of the agent, occasionally after 4-5 yr. After intraosseous inj. of DMBA to 8 dogs (6 male, 2 female), no tumors developed after periods of observation up to 13 yr. After admin. of 8 mg, in one dog there was osseous fibrosis at the site of inj. and a moderate hyperplasia of testicular tissue; in another there was atypical growth of endometrial epithelium without changes in the endometrium. DMBA (15 mg) inj. into 4/8 dogs produced 1/4 osseous tissue fibrosis at the site of inj. and fatty degeneration in the liver; 1/4 there developed cancer of the thyroid gland with destruction of vessels with resultant hemorrhages; in 1/4 thyroid gland cancer, carcinoma of the left testicle and atypical epithelial growth in the urinary bladder were observed; in 1/4 there was metastatic thyroid cancer and a metastatic seminoma. 20-Methylcholanthrene (20-ME; 10 mg) caused atypical changes in the prostatic tissue with lung metastasis of the same structure in 1/8; cause of death 12 yr. 10 mo. after initiation of experiment was prostatic cancer with large metastases of both lungs; in 1/8 20-ME (20 mg) induced marked liver cirrhosis without local changes. Survival time of the dogs used in this study was equivalent to that of rabbits, 15 yr.

047 CARCINOGENIC ACTIVITY OF SOME METHYLATED HOMOLOGS OF 1,2-BENZANTHRAcene. (Fr.) Lacassagne, A., F. Zajdela, B. Buu-Hoi and O. Chalvet. Bull. Ass. Cancer 49(3):312-319, 1962.

Male and female mice, strain XVII nc/Z from the Radium Institute were inj. with each of the derivatives of 1,2-benzanthracene (0.6 mg x 3 times in 2 ml sterile, neutralized olive oil, at weekly intervals, s.c. in the flank). Results were compared to Mason indexes of carcinogenicity based on hydrocarbon tendency to form complexes by charge transfer) which on a theoretical basis postulates as carcinogenic compounds with indexes of 1.334-1.446. 3'-Methyl- and 4'-methyl-1,2-benzanthracene with indexes of

1.454 and 1.448 induced sarcomas in 0/62 and 1/62 mice, resp. 1',9-Dimethyl-1,2-benzanthracene, with a Mason Index of 1.4287 induced sarcomas in 14/48 mice with a mean latency of 256 days. 4-Methyl- and 3-methyl-1,2-benzanthracene induced sarcomas in 56/64 and 22/65 mice with mean latencies (males, females) of 136, 158 and 235, 216 days) and low indexes of 1.441 and 1.439, resp. The prototype, 3,4-benzpyrene, induced tumors in 100% of 316 mice and had a Mason Index of 1.410.

63-1048 HISTOLOGIC AND HISTOAUTHORADIOGRAPHIC PICTURE OF EXPERIMENTAL GASTRIC CARCINOMA. (Ger., Abstract) Toledo, J. D. Klin. Wschr. 41(10):519, 1963.

The preventriculi of rats receiving N-nitroso-N-methylurethan (0.01% soln. in drinking water) were examined at regular intervals between days 2-320. Carcinoma developed through definite stages: necrosis of the forestomach epithelium (which became covered by reepithelialized epithelium) was followed by hyperplasia and development of papillomas; with more dilute soln., hyperplasia and papillomas developed without preceding necrosis. Later, papillomas increased in size and in the deeper layer of the epithelium, proliferative changes which led to early stromal invasion were observed; this transition to carcinoma developed by 320 days. The autoradiographic studies of DNA metabolism (utilizing tritiated thymidine) showed that from the beginning the number of DNA synthesizing cells was greatly increased and remained high during the whole time of tumor development. The transition to carcinoma was characterized by spread of the label throughout the whole epithelium. The diploid DNA values of normal basal cells increased after 3 days to tetraploid, and later to almost octaploid values; subsequently during regeneration and hyperplasia of the epithelium, the values gradually decreased. These results confirmed the finding that development of carcinoma is not sporadic but is regulated in a specific manner. When these findings are compared with the biochemical actions of alkylating carcinogenic compounds (to which this agent belongs), it was supposed that a disturbance of the DNA-RNA-protein regulating system of the cell occurred, and the resulting release of DNA-proliferation was the cause of malignant growth.

63-1049 THE ACTION OF EMBRYONAL HOMOGENATES OF VARIOUS AGES ON A CHEMICALLY INDUCED SARCOMA OF CHICKEN. (Ger.) Seilern-Aspang, F. (Austrian Inst. Cancer Res., Vienna) and M. Weissberg. Acta Biol. Med. Germ. 10(3-4):439-442, 1963.

After admin. to chickens of dibenzanthracene (24 mg, 2.4% soln., in benzene, i.m.) 57/90 developed spindle cell sarcomas at the site of inj.

after 44 days to 12 mo. The center of the tumor was always necrotic and death occurred invariably 1-3 mo. later in animals that received no further treatment. All had lung metastases, about 80% had liver, and 20% had kidney metastases. In further experiments, some tumor regression was obtained with chicken embryo homogenates; egg white from eggs incubated 2-5 days was without effect.

- 63-1050 KINETICS OF EPIDERMAL CELL PROLIFERATION IN EXPERIMENTAL SKIN CARCINOGENESIS. (E.) Evensen, A. (Inst. Gen. Exp. Path., Oslo, Norway). *Bull. WHO* 28(4):513-515, 1963.

The mitotic duration (MD) of epidermal cells of hairless mice after admin. of colchicine at 8 A.M. and sacrifice at 2 P.M., was 1 hr.; mitotic rate (MR) was 0.57%/hr.; DNA synthesizing time (ST) between 9 and 10 A.M., utilizing tritiated thymidine, was 5.3 hr.; DNA synthesizing rate (SR) was 0.55%/hr. In the 24 hr. after application of 20-methylcholanthrene (20-Me; 1% in benzene, 0.005 ml), MD was 0.25 hr.; MR 1.72%/hr.; ST 1.1/hr.; and SR 1.68%/hr.; after 11 days MD was 2 hr.; and MR 0.62%/hr. These marked variations in epithelial cell proliferation caused by 20-Me do not, however, allow calculation of MR or SR unless MD and ST are constant and not influenced by treatment. From a study of the epidermal mitotic count observed in untreated mice at intervals over a 24 hr. period, it was concluded that rhythmic variations in mitotic count are due to variations in MD and not in MR.

- 63-1051 PRECANCEROUS CHANGES IN MUSCLE CELLS EXPOSED TO NICKEL SULPHIDE. (E., Abstract) Gilman, J. P. (Dept. Anat., Ontario Vet. Coll., Guelph, Ont.) and P. K. Basrur. *Proc. Am. Assn. Cancer Res.* 4(1):23, 1963.

The histologic changes occurring in rats after implantation i.m. of nickel sulfide discs were compared to those occurring in controls implanted with FeO discs. Within 4-5 wk. after the initial inflammatory reaction, rat tissues adjacent to FeO returned to normal. However, cells surrounding Ni_3S_2 discs exhibited a variety of progressive changes including increasing numbers of vesiculated subsarcolemmal nuclei, nuclear rowing and clustering, nucleolar enlargement, margination of the nuclear membrane, and extrusion of Feulgen-positive material into the cytoplasm. Prior to wk. 8 mitotic stages were infrequent, but thereafter there was longitudinal splitting of multinucleated muscle fibers giving rise to uni- and binucleated myoblast-like cells, some faintly striated. The mitotic frequency increased with time, giving rise to areas of progressively less well differentiated cells. Typical rhabdomyosarcomas

developed in 4-6 mo. in 70%-80% of the animals. Tissues exposed to Ni_3S_2 for 11 or more wk., when transplanted into weanling rats, caused typical rhabdomyosarcomas. (See also CRA 1(1): #119, 1963.)

- 63-1052 LOCALIZATION OF C^{14} -LABELED DIMETHYLBENZANTHRACENE (DMBA) IN RAT LIVER MITOCHONDRIA. (E., Abstract) Wong, T.-W. (Dept. Path., U. Chicago, Ill.), G. Catravas, and N. C. Yang. *Proc. Am. Assn. Cancer Res.* 4(1):73, 1963

Administration of 9,10-dimethyl-1,2-benzanthracene C^{14} (DMBA; 10 μC mixed with 20 mg carrier DMBA in sesame oil, intragastric) to female Sprague-Dawley rats revealed that at 3-72 hr. after feed 12%-43% of the compound was present in the liver mitochondria, with a max. at 6 hr. Attempts at localization of the DMBA by spectrofluorometry were complicated by severe quenching of the DMBA fluorescence by cellular constituents.

- 63-1053 EXPERIMENTAL CANCER OF THE UTERINE CERVIX IN THE MOUSE AND ITS CONDITIONING BY ESTROGENS. (Fr.) Laffargue, P. (Fac. Med. Marseille, France), A. Samso, R. Luscan and H. Francois. *Ann. Anat. Path. (Paris)* 8(1): 85-108, 1963.

Female mice aged about 6 mo. (Pasteur Inst. strain Ardenny strain, or a homogeneous hybrid strain) were implanted with a small pellet of 20-methylcholanthrene (20-Me; 0.8 mg in 3-4 mg cholesterol) in the cervix and examined periodically for tumor progression by colposcopic, histologic and macroscopic methods. These studies confirmed the progression from dysplastic, to intraepithelial, to invasive carcinoma. The first carcinomas were detected at 60 wk. in 4/10 mice, with 1/10 showing carcinoma *in situ*. At 100 wk. there were 16 carcinomas, 15 carcinomas *in situ* and 8 dysplasias in 65 mice studied. In mice castrated at 4-6 wk. and then implanted with 20-Me there were 1 microcarcinoma and 2 carcinomas *in situ* among 10 animals at 40 wk., and at 100 wk., among 61 mice, the number of cancers and carcinomas *in situ* were 24 and 6, resp. When mice were castrated and then treated with estradiol benzoate (benzogynestryl; 0.008 mg every 3 wk. in olive oil s.c.) the first carcinomas appeared at 60 wk. in 4/10 mice, with 1/10 showing dysplasia. By 100 wk. there were 14 epitheliomas, 11 carcinomas *in situ*, and 12 dysplasias in 67 mice. The increased frequency of carcinomas in the castrated mice, together with the low frequency of dysplasias and carcinomas *in situ* leads to the hypothesis that carcinomas of the cervix may be due to uncontrolled proliferation of a reversible intraepithelial lesion which follows removal of estrogens.

- 63-1054 EFFECT OF CYCLOPHOSPHAMIDE ON EMBRYO FORMATION. (Fr.) Gerlinger, P.

. Med., U. Strasbourg, France), J. V. Ruch
J. Clavert. C. R. Soc. Biol. (Paris) 157(1):
177, 1963.

phosphamide (0.1 mg in 0.2 ml Tyrode soln.
inj. into the albumen of chick eggs prior
incubation for up to 16 days. Frequency of
living fetuses fell from 88.5% of 25 at 3
to 3% of 90 at 16 days. On morphologic
ination after 7 days the surviving fetuses
) appeared normal, but at 9 days all the
ivors (50%) showed moderate hypotrophy.
des hypotrophy, 11 day survivors also
ed a 59% incidence of abnormalities (34%
typical, 25% were atypical). By 14 days
23% of 80 chicks survived; only 20% of these
ented abnormalities, none typical. The
rved changes were paralleled by decreased
gain in treated embryos, starting at about
9, and leading to a 16-day mean embryo wt.
.90 g for treated compared to 13.9 g for
al embryos.

055 EXPERIMENTAL CARCINOGENESIS BY 4-
NITROQUINOLINE N-OXIDE (4NQO).

Abstract) Tanaka, T. (City Hope Med.
, Duarte, Cal.), T. Kakefuda and R. Kinoshita.
Am. Assn. Cancer Res. 4(1):67, 1963.

ection of young ICR mice with 4-nitro-
oline N-oxide (NQO; 0.5 mg i.p. in propylene
ol) caused generalized lymphomas appearing
9-304 days in 6/14. Weekly i.v. inj.
mg) produced lymphomas in 1/20 mice; weekly
inj. (0.03 mg) caused breast cancer in 1/20.
newborn mice NQO (0.03 mg x 1 in gelatin
ne) caused lymphomas in 9/27 mice which
ared between days 204-318; spindle cell
omas appeared on day 302 in 2/27. No lympho-
were observed in 176 untreated ICR controls.
lymphomas were transmissible to ICR mice
n cell-free preparations from the original
rs, their transplants, and cultures. All
e materials contain A and C type virus
icles, and transitional forms between the
ypes, in the cytoplasm and outside the cells.
57B1 mice NQO (0.01 mg/wk. i.p. in cotton
caused spindle cell sarcomas in 12/16,
reas the same dose in propylene glycol, inj.
caused no tumors in 15 animals observed
over 300 days.

056 LEUKEMIA IN CBA MICE AFTER TRANS-
PLANTATION OF A METHYLCHOLANTHRENE
-INDUCED HEPATOMA. (E., Abstract) Liebelt, R.
Texas, M. D. Anderson Hosp., Houston),
Liebelt, L. Dmochowski and J. Sykes. Proc.
Assn. Cancer Res. 4(1):38, 1963.

0-methylcholanthrene-induced hepatoma, trans-
nted into young CBA mice, grew in 4/7. Three
the hepatoma-bearing and 3 negative mice
eloped hepatosplenomegaly and stem cell leu-
ia at 250 days. No leukemic foci were found

in the original hepatoma. Transplants of leukemic
spleens caused hepatosplenomegaly with elevated
WBC counts in all hosts. Incidence of reticular
cell neoplasms was 2% in controls. The 2nd trans-
plant generation of the hepatoma grew in 3/16
mice who were all negative for leukemia at 171-311
days. However, all of the remaining 13 mice who
showed only temporary hepatoma development, had
leukemias at 137-316 days. The third hepatoma
transplant generation grew in all mice and none
developed leukemia between 159-216 days. The
4th transplant generation grew in all mice; 4 of
these had their tumors excised at 123 days, and
all developed leukemia 137 days later. The re-
maining, tumor-bearing mice died free of leukemia
at 240 days. The hepatoma grew in all mice in its
5th transplant generation, and none had leukemia
at death (230 days).

63-1057 NATURAL HISTORY OF PRENEOPLASTIC AND
NEOPLASTIC LESIONS OF THE LIVER IN

RATS FED N-2-FLUORENYLDIACETAMIDE. (E., Abstract)
Reuber, M. D. (Beth Israel Hosp., Boston, Mass.).
Proc. Am. Assn. Cancer Res. 4(1):56, 1963.

Serial biopsies on Wistar or inbred AXC male rats
fed N-2-fluorenyldiacetamide (0.025% in a semi-
synthetic diet for 4 wk. alternating with 1 wk.
of basal diet for up to 36 wk.) showed areas of
hyperplasia at 9-12 wk., nodules of hyperplasia
at 12-20 wk., hepatomas 5 mm in diameter or less
at up to 25 wk., and well developed hepatomas at
32-36 wk. In 14 rats with areas of hyperplasia
after 9 wk., the livers of 8 survivors were nor-
mal at the end of 65 wk., whereas 10/10 animals
developing hyperplasias at 12 wk. had nodules at
65 wk., and 2/10 had small hepatomas. All animals
with nodules or hyperplastic areas at 14 wk.
died with hepatomas at approx. 84 wk., but rarely
with metastases, whereas animals with nodules at
20 wk. died of hepatomas at an av. of 68 wk.
(50% with metastases). On short exposure to the
carcinogen, the areas of hyperplasia were re-
versible, and even on longer exposure only small
areas evolved into nodules or hepatomas. In
animals with hepatomas, tumor growth rate was
correlated directly with presence of metastases,
and inversely with morphologic differentiation
and survival of the animals.

63-1058 N- AND 7-HYDROXY-2-FLUORENYLACETAMIDE,
MAJOR METABOLITES OF N-2-FLUORENYLACETA-
MIDE IN HUMANS. (E., Abstract) Weisburger, J. H.
(NCI, Bethesda), N. H. Steigbigel, P. H. Grantham,
E. C. Vanhorn and E. K. Weisburger. Proc. Am.
Assn. Cancer Res. 4(1):70, 1963.

Five male pts. with a variety of diseases (carci-
noma of lung, mycosis fungoides, multiple myeloma,
chronic myelogenous leukemia, and teratocarci-
noma of the testis) all converted N-2-fluorenyl-9-
C14-ylacetamide (0.3 mg = 107 cpm., p.o.) to the
proximate carcinogen, the N-hydroxy derivative.
At 96 hr. 73-108% of the dose was in the urine;

46-74% appeared during the first 12 hr. The urinary metabolites were classified as: free = 2.7-4.4%, glucosiduronic acids = 38-59% (of which 11-32% was N-hydroxy-2-fluorenylacetamide, and 57-77% was N-(7-hydroxy-2-fluorenyl)acetamide) and sulfuric acid esters = 3.1-9.3%. The presence of the N-hydroxy-derivatives was confirmed by isotope dilution and by ion-exchange chromatography.

63-1059 ANTIBIOTICS AND CONGENITAL MALFORMATIONS. (E.) Carter, M. P. and F. Wilson. *Lancet* 1:1267-1268, 1963.

In a series of 656 pregnancies from 2 practices, 1955-62, pregnancy wastage for the whole series was 15.6%, including 17 mothers who had been prescribed an antibiotic in the first 12 wk. of pregnancy; pregnancy wastage after a febrile illness in the same period (excluding rubella) was 14.7% of all pregnancies so affected. The pregnancy wastage rate was also increased after aspirin, salicylates, trifluoperazine, amphetamines and sex hormone preparations; but not after other drugs, particularly sulfonamides and "Ancoloxin". Other recent reports are also briefly reviewed.

63-1060 AUTORADIOGRAPHIC LOCALIZATION OF TRITIUM LABELED AZO DYE IN RAT LIVER. (E., Abstract) Spain, J. D. (Dept. Chem., Mich. Coll. Mining and Technol., Houghton) and J. Brouillard. *Proc. Am. Assn. Cancer Res.* 4(1):65, 1963.

3'-Methyl-DAB was prepared from dimethylaniline and tritiated m-toluidine and given for 1 wk. in the diet to rats (0.06%, specific activity = 110 mC/g) that had been fed previously unlabeled dye for 0-11 wk. On microautoradiography bile duct cells and cholangiofibrosis contained essentially no dye, while central zones of liver lobules contained dye in significantly larger quantities than portal zones. The results on tumor conc. to date are considered inconclusive.

63-1061 INDUCTION AND PROGRESSION OF 3,4,9,10-DIBENZPYRENE-INDUCED SUBCUTANEOUS SARCOMAS AS AFFECTED BY CHEMOTHERAPY AND CALORIC RESTRICTION. (E., Abstract) Homburger, F. (Bio-Res. Inst., Cambridge, Mass.) and A. Treger. *Proc. Am. Assn. Cancer Res.* 4(1):29, 1963.

In C57Bl/6 mice inj. with 3,4,9,10-dibenzpyrene (500 µg in peanut oil) methotrexate (no details) given 5 wk. after sarcoma induction had no effect on frequency of tumors or rate of tumor growth, and little effect on established 1 cm tumors, but prolonged survival time. Thio-tepa inj. (0.1 mg x 11 during 1 mo.), beginning 5, 6 and 7 wk. after carcinogen inj., or when tumors measured 1 cm., slowed tumor growth temporarily and had significant effects on

established tumors. Caloric restriction (to less than 2.5 g of Purina pellets/day/mouse) slowed the rate of tumor formation, did not affect growth of established tumors, but prolonged survival time from 27 days (after tumors had reached 1 cm) in untreated controls, to 36 days.

63-1062 STUDY OF POLLUTION OF THE NORTH SEA AND ARCTIC OCEAN BY POLYAROMATIC HYDROCARBONS OF THE 3,4-BENZPYRENE TYPE. (Fr.) Mallet, L. (Munic. Lab., Police Dept., Paris), Perdriau and S. Perdriau. *Bull. Acad. Nat. Med. (Paris)* 147(14-15):320-325, 1963.

Samples of sands and biological specimens collected during an oceanographic survey were analyzed for pollution with 3,4-benzpyrene by chromatography and spectroscopy. Significant amounts of the carcinogen (over 10 µg/100 g after hydrolysis) were found in mussels (up to 23 µg/100 g), and starfish, and lesser amounts were detected in soles, eels, crabs and other crustaceans. Pollution was greater in sands and specimens from the areas south of the North Sea (up to 176 µg/100 g).

63-1063 PROGESTERONE AS A FACTOR IN METASTASIS. (E., Abstract) Poel, W. E. (Weizmann Inst. Sci., Rehovoth, Israel) and N. Haran-Ghera. *Proc. Am. Assn. Cancer Res.* 4(1):53, 1963.

Normal LAF-1 female mice bearing the Furth mammary pituitary tumor (MtT) under regulated growth conditions (implanted s.c., excised when 15 mm, then a fragment re-implanted) for 20, 30, 38 or 54 wk. before final excision had incidences of pulmonary and thoracic metastases from MtT of less than 17%. However, when the animals bearing the MtT for 30 wk. were also treated with progesterone (1% s.c. 6 days/wk. during the last 4 mo. of tumor growth), the incidence of MtT metastases increased to 75%. Results indicate that progesterone may promote metastases from pre-existing solid tumors.

63-1064 THE NEOPLASTIC NATURE OF LIVER "BLOOD CYSTS" INDUCED BY URETHAN. (E., Abstract) Trainin, N. (NCI, Bethesda). *Proc. Am. Assn. Cancer Res.* 4(1):67, 1963.

Liver "blood cysts" induced in C57Bl/6 mice by inj. of urethan (20 mg/wk. x 10) were transplanted i.m. in C57Bl/6 animals. All 20 recipients (of both sexes) showed progressive growth at the site of inj., with a latent period of 3 mo. Microscopically the tumors were hemangiomas and have proven transplantable, with a decrease in latency in successive transplant generations.

63-1065 ATTEMPTS AT IMMUNOPROPHYLAXIS OF EXPERIMENTAL CANCERS. (Fr.) Maisin, J.

Inst., Catholic U. Louvain, Belgium).
Un. Int. Cancr. 19(1-2):94-98, 1963.

adult rats, inj. of a microsomal fraction from
h or formaldehyde inactivated (17.5% soln.,
x 12 hr.) dimethylaminoazobenzene (DAB)-
uced hepatomas decreased the frequency of
tomatos induced by DAB (given for 8 mo., p.o.)
approx. 50% to 20-25% at 70 wk.; the micro-
somes were inj. s.c. 5x before DAB treatment,
then 1x/mo. during treatment. In similar
iments rats were inj. s.c. with a microsomal
tion from 20-methylcholanthrene (MC)-in-
d sarcomas for 5x before MC treatment (0.2
f a 1/400 soln. in benzene, s.c.) or 5x
re MC treatment, and then 1x/mo. x 55 wk.
5 wk. the frequency of sarcomas was approx.
in untreated controls, 60% in rats inj.
microsomes before, and 40% in rats inj. both
re and after MC treatment. There was a lag
bout 10 wk. in the appearance of tumors in
ted compared to control rats. In adult
, inj. of microsomes 5x/wk. s.c. before MC
painting (3/wk. to a total of 23 treatments)
owed by microsome inj. (1x/mo. x 300 days) re-
d the frequency of MC-induced skin cancers at
days from 65% for controls to 54%, 41% and 38%
fresh microsomes from DAB-induced rat
tomatos, formalin-inactivated microsomes from
induced rat heptatomas, and microsomes from
ich carcinomas, resp. Similar results were
ined in 2 separate experiments. However,
le inj. of newborn mice with microsomes
Ehrlich carcinomas or from DAB-hepatomas
owed at 3 1/2 mo. by skin painting with MC
above) increased the frequency of skin cancers
00 days from 65% in controls to 85% and 82%,

066 CANCEROGENIC SUBSTANCES IN WATER AND
SOIL. XIII. EXPERIMENTS IN MICE FED
BENZOPYRENE, MINERAL OIL AND DETERGENTS.

) Borneff, J. (Inst. Hygiene, Mainz,
any). Arch. Hyg. Bakt. 147(1):28-40, 1963.

ries of 400 mice were fed for 500 days with
benzpyrene (BP; approx. 0.6 mg/kg/day,
10 mg/mouse), detergent (D; liquid Pril,
35-40 g) and Esso mineral oil (MO; total
). The animals were divided in 8 groups of
each and treated as follows: Group I, normal
, D and MO in drinking water; Group II, BP
feed, D and MO in water; Group III, normal
, D, MO and BP in water; Group IV, normal
and normal water; Group V, normal feed and
water; Group VI, normal feed, D and BP in
r; Group VII, BP and MO in feed, normal
r, and finally, Group VIII, BP and MO in
and D in water. The incidence of patho-
cal findings increased in the following se-
ce: I, IV, V, VII, VIII, II, VI, III.
gnant tumors and large papillomas were
icularly high in Groups III and VI, with an
dence of 83% and 57.5%, resp., against an
incidence of 12.5% for all other groups.

Carcinomas of the phrenic ampulla of the esophagus
developed only in these two groups. BP in the
solid food, even in the presence of MO and D,
induced only hyperkeratoses and papillomata.
Aqueous solutions of MO stabilized with detergents,
while affecting the general health of the animals,
did not modify the effect of BP admin. in the
feed. It is concluded that residues of household
detergents may not influence the effect of carci-
nogenic substances present in food, but that
emulsifying agents present in homogenized food
articles may enhance the effect (in the stomach)
of carcinogenic compounds.

63-1067 SARCOMAS AT THE SITE OF SUBCUTANEOUS
INJECTION OF TRYPAN BLUE IN THE WHITE
RAT. II. ELECTRON MICROSCOPE CYTOLOGIC STUDY.
(Fr.) Driessens, J. (Inst. Cancer Res., Lille,
France), A. Dupont and A. Demaille. C.R. Soc.
Biol. (Paris) 157(1):128-130, 1963.

Electron microscopic study of previously described
tumors (see in CRA 1(2):#234, 1963) confirmed
their polymorphic nature. The cells varied from
20-45 μ in height and were separated by a dense
fibrillary stroma. The cytoplasm was often
vacuolated and the nuclei were large and surrounded
by a double membrane. The nucleoplasm was homoge-
neous, and contained a single or double nucleolus,
rather dense, and often showing a beehive
structure. Mitochondria were scarce; they often
contained irregular cristae. The ribosomes were
frequently aggregated in clumps of 4-6 elements
and the cytoplasm contained numerous vacuoles
surrounded by a single membrane covered with
ribosomes. Some other smaller vacuoles resembled
the outer cell membrane and suggested involvement
in pinocytosis. The stromal fibers were in close
contact with the cells, from which they appeared
to be derived, and were without regular striations
or external membranes.

63-1068 AZO DYE HEPATOMA OF THE WHITE RAT. III.
ELECTRON MICROSCOPE CYTOLOGIC STUDY:
PRE-HEPATOMA HEPATITIS. (Fr.) Driessens, J.
(Inst. Cancer Res., Lille, France), A. Dupont and
A. Demaille. C.R. Soc. Biol. (Paris) 157(1):
123-125, 1963.

Liver lesions, induced in Wistar rats by 3'-methyl-
D.A.B. (not otherwise specified, but see CRA
1(2):#221, 1963), 5 mg/day plus a carcinogenic diet
similar to one previously described, were ex-
amined by electron microscopy at weekly intervals
for 5 wk. In the cytoplasm the mitochondria ex-
hibited progressive swelling from the 3rd wk. of
treatment, the ergastoplasm disappeared at about
1 wk. or was reduced to dilated sacs filled with
Palade's granules. These changes were followed
at about 3 wk. by cytoplasmic edema and vacuoli-
zation accompanied by loss or decrease in the
number of mitochondria. Some cytoplasmic granules
found after 2 wk. of the carcinogenic diet, in-
cluded glycogen, lipid, siderous, and ribonucleic
acid aggregates. In the intracellular spaces

edema was observable after 2 wk. Biliary hyperplasia was not observed until 5 wk. and consisted of multiplication of clear cells with large nuclei and little cytoplasm, surrounding capillaries provided with many microvilli in the walls. These changes agree with microscopic changes classified as "clarifying hepatitis" and thought to be precancerous in D.A.B.-fed mice.

63-1069 EXPERIMENTAL STUDY OF THE RELATIONSHIP BETWEEN VITAMIN B₁₂ AND TWO ANIMAL TUMOUR SYSTEMS. (E.) Rigby, C. C. (Hosp. for Sick Children, London) and M. Bodian. Brit. J. Cancer 17(1):90-99, 1963.

August strain rats with transplanted fibrosarcoma PWA2, treated with massive doses of cyanocobalamin (vitamin B₁₂; 5 µg/day x 8 days; or 30 µg/day for life span of 5-7 wk.) led to increase of tumor growth by 200% and increase of vitamin content of the tumor by 55%. Similar treatment of CAF1/JAX mice, with implanted C1300 neuroblastoma led to a decrease in tumor growth of 23% and a 90% increase in tumor vitamin content.

63-1070 PRODUCTION OF CANCER IN MICE BY MEANS OF DIETHYLNITROSAMINE. (Ger.) Schmäh, D. (Inst. Path., U. Bonn/Rhein, Germany), C. Thomas and K. König. Naturwissenschaften 50(11):407, 1963.

The LD₅₀ of diethylnitrosamine in mice was found to be 180 mg/kg in a single s.c. inj. The animals died of necrosis and bleeding of the liver parenchyma 2-6 days following the inj. Of 28 DBA mice (age 3-4 mo.), given a daily dose of 13 mg/kg (in drinking water) until death, all developed malignant tumors of the liver. There was no difference in the wt. curve as compared to controls. The av. induction time was 180 ± 28 days, with an av. total ingested dose of 2,343 ± 360 mg/kg. None of 18 controls developed tumors during the period of observation. Histologically, the tumors appeared to be partly solid and partly reticular hemangiosarcomas, surrounded by typical benign hepatomas. Occasional lung metastases were found. No well defined liver cell carcinomas were found, and, in contrast to rats, no signs of cirrhosis were encountered.

63-1071 THE EFFECT OF 1:2:5:6 DIBENZANTHRACENE (D.B.A.) UPON THE METABOLISM OF β-NAPHTHYLAMINE IN THE RAT. (E.) Dewhurst, F. (Mt. Vernon Hosp., Northwood, Middlesex, England). Naturwissenschaften 50(11):404-405, 1963.

When five 10-month-old male Wistar rats were inj. i.p. with 30 mg of β-naphthylamine HCl, 24 hr. after prior treatment with 1,2,5,6-dibenzanthracene (DBA; 1 mg i.p.) they excreted 26.3% 2-amino-1-naphthol compared to 21% for 11 control rats not given DBA. In ten 6-week-old male rats

inj. i.p. with 10 mg β-naphthylamine after treatment with DBA, excretion was 23.4% (controls 18.1%); for ten female 6-week-old treated rats was 27.0% (controls 15.8%). The stimulation of carcinogenic metabolites appeared to be stimulated more in young animals than old, and more in young females than young males.

63-1072 INDUCTION OF TUMORS IN THE SYRIAN HAMSTER WITH DIETHYLNITROSAMINE (N-NITROSODIETHYLAMINE). (E.) Herrold, K. M. (Lab. Path. NCI, Bethesda) and L. J. Dunham. Cancer Res 23(5):773-777, 1963.

Among 28 hamsters treated intragastrically with diethylnitrosamine (DENA; 0.4% in water, 0.4 ml x 2/wk., up to 7 mo.) the following tumors developed: trachea 28, bronchi 10, liver 22, ethmoturbinals approx. 10, and kidney 12. Of 26 hamsters treated intratracheally (1:14 in water, 0.5 ml 1 x/wk. up to 6 mo.) tumor incidences were trachea 25, bronchi 14, liver 0, ethmoturbinals 4, and kidney 0. The tumors in the intragastric DENA group were hepatocellular carcinomas. (See also CRA 1(5):#884, 1963.)

63-1073 TERATOGENIC EFFECTS OF ORGANIC COMPOUNDS. (1). A METHOD FOR LABORATORY TESTING. (Ger.) Riemschneider, R. (Inst. Biochem. Free U. Berlin-Dahlem, Germany), K. Brockmeyer and H. Sommer. Zschr. Naturforsch. (B) 18(2):167-168 1963.

Pregnant, 12-13-month-old rabbits of a strain developed by K. Lange received N-phthalyl glutamic acid amide, 200 mg/kg/day, p.o. from day 7-14 of pregnancy, followed by approx. 150 mg/kg/day, p.o. through day 18 (total dose: 2.2 g/kg). The gestation period ranged from 30-32 days, and the birth wt. of the young ranged from 48-61 g. Teratogenic effects were demonstrable in the offspring of 12/88 treated animals, consisting primarily of shortening of the forelegs and various (unspecified) defects of the hind limbs comparable to congenital abnormalities induced by thalidomide or related compounds in man. In treated animals, 2/12 litters contained 3 and 4 offspring, the remainder 6-9; in 6 controls, litter size was 6-9. In treated animals, there were 12/81 fetal deaths, 53 showed abnormalities. Among 6 control animals, litters averaged 7, ranged from 6-9, with 1/43 born dead and with no congenital abnormalities. A previous attempt to induce teratogenesis with the same compound, in 85 rabbits, had been entirely unsuccessful. In a concurrent experiment, a comparable group of rabbits was given the C¹⁴-labeled compound, 30 mg/kg, p.o. on day 15 of pregnancy; products of hydrolysis and/or metabolic breakdown were demonstrable in the fetus and the amniotic fluid within 90 min.

63-1074 EXPERIMENTAL STUDY ON PULMONARY CANCER. (Jap.) Yamada, M. (Nat'l. Osaka Hosp.,

n) and T. Yamanake. Gan No Rinsho (J. Cancer Clin.) 9(3-4):168-169, 1963.

pellets of 20-methylcholanthrene (20-Me; mg with an equal amount of carbowax 4000 cholesterol) were implanted into the pulmonary parenchyma of Wistar rats, proliferation of epithelial cells was noted after 5-7 days. In another series, electrocauterized sites were studied. When 20-Me pellets were implanted in the sites immediately, 1 wk. or 1 mo. after cauterization, proliferation of the epithelial cells and stratified squamous cells of the bronchiole wall became noticeable after 2-3 wk., 1 wk. or 1 mo., resp. The authors state that the reason for the retardation in appearance of proliferative growth where 20-Me was combined with cauterization was obscure.

1075 EXPERIMENTAL INDUCTION OF PULMONARY CARCINOMA. (Jap.) Takizawa, E. (Dept. Path., U. Chiba Sch. Med., Japan) and Kanizawa. Gan No Rinsho (Jap. J. Cancer Clin.) 9(4):172-173, 1963.

p-benzoquinone (10 mg/day over a 6-hr. period x 60 days) was admin. by inhalation to 60 strain A mice. In 9 experimental animals, infiltrative hyperplasia was seen with marked hyperchromaticity of the nucleus (especially the nuclear membrane) and marked basophilia of the protoplasm. In 9 of 60 adenoma seen in 60 controls, these changes were not seen. In the experimental group, the cells were larger than those in the control group. Thus the drug induced malignant changes similar to those seen in human lung cancer.

1076 HISTOCHEMICAL STUDY ON EXPERIMENTAL INHALATION OF p-BENZOQUINONE. I. TISSUE OF MICE, WITH EMPHASIS ON PERIPHERAL BRONCHIOLES. (Jap.) Hayashi, Y. (Dept. Pathol., U. Sch. Med., Japan), N. Kanizawa and E. Kanizawa. Gan No Rinsho (Jap. J. Cancer Clin.) 9(4):167-168, 1963.

admin. by inhalation of p-benzoquinone (10 mg over a 3-hour period, 2x/day, 6 days/wk.) to strain A mice, lung tissue, especially bronchiolar epithelium and interstitial tissue, was studied histologically and histochemically at 20, 60, 120 and 200 days of treatment. At 120 days there was slight atypical proliferation in the bronchioles in 8/8 and an adenoma in 1/8; only hypertrophy was found in bronchiolar epithelium. Feulgen-positive material in the bronchioles increased 200 days after inhalation. Alkaline phosphatase activity was weakly positive in the basal membrane of bronchiolar epithelium at 120 and 200 days. PAS-positive mucopolysaccharides disappeared from the basal membrane at 120 days; no changes were observed in succinate dehydrogenase activity.

63-1077 X-RAY STUDY ON THE DEVELOPMENT OF EXPERIMENTAL PULMONARY CANCER IN RATS. (Jap., Abstract) Imagawa, U. (Dept. Int. Med., Sch. Med., Tokyo Dent. Med. Coll., Japan), K. Takemoto, K. Namie and H. Hajikano. Gan No Rinsho (Jap. J. Cancer Clin.) 9(3-4):169-170, 1963.

Nonfatal tuberculosis was produced in female rats (Saitama strain) by inoc. with tubercle bacilli (KH2Rv or Ravenell strain, i.v.) 1 mo. before infusion with AAF (acetylaminofluorene?; 5 mg/day, total over 500 mg). X-ray examination revealed no significant difference in tumor incidence (4/13) compared to a group inoc. with tubercle bacilli 1 mo. after AAF (3/13). While areas of scar tissue in tuberculous rats were not frequent, they were believed to be the site of induced tumors. In groups of rats given 20-methylcholanthrene (3 mg intratracheally), NiO (no dose), or 3-4 B.P. (3,4-benzpyrene?; 5 mg intratracheally), X-ray shadows in the left middle lobe were seen after 2-3 mo. Histological examination of the epidermis showed marked hypertrophy followed by malignant infiltration into surrounding tissue in 50% of rats after 3 mo.

63-1078 INFLUENCE OF p-HYDROXYPROPIOPHENONE ON LIVER TUMORIGENESIS IN RATS INGESTING ETHIONINE AND N-2-FLUORENYLACETAMIDE. (E.) Sidransky, H. (Dept. Path., Sch. Med., U. Pittsburgh, Pa.), S. Clark and T. Baba. J. Nat. Cancer Inst. 30(5):999-1008, 1963.

Inbred Osborne-Mendel rats were fed a diet containing DL ethionine (E; 0.25%) or N-2-fluorenylacetamide (2-FAA; 0.025%) with or without p-hydroxypropiophenone (PHP; 1.5%). In chronic experiments PHP + 2-FAA had no inhibitory effect on the induction of liver tumors, with 10/10 hepatocellular carcinomas compared to 6/11 in 2-FAA controls. PHP + E, however, resulted in a marked decrease in the number of carcinomas, 1/13 compared to 10/18 in E controls. Rats fed E + PHP developed severe cholangiofibrosis throughout the liver (in 13/13). In short term experiments, rats fed the E diet (with or without PHP) had large decreases in liver glycogen content and ductular cell proliferation, more marked at 4 and 6 wk. in the E + PHP, than the E group. Results suggest that ductular cell proliferation leads to cholangiofibrosis, but do not support the view that cholangiofibrosis is a precancerous lesion.

63-1079 INDIVIDUAL SMOKING BEHAVIOR AS A SIGNIFICANT PARAMETER IN THE OVERALL EFFECTS. (Ger.) Waltz, P. (Fabriques de Tabac Reunies, Neuchatel-Serrieres, Switzerland) and M. Häusermann. Zschr. Praeventivmed. 8(2):99-110, 1963.

In addition to variables such as the type of tobacco and the physical characteristics of the

cigarette, filter and paper, the amount of condensate to which a smoker is exposed is affected by his smoking behavior. Thus, the number of puffs may vary from 4-20 per cigarette, the volume of the puff may vary from 17-51 ml, the stub may be anywhere from 16-36 mm and, although the duration of a single puff varies little, variations in the negative pressure curve during the puff may produce a 10% variation in the amount of condensate produced. In addition, inhalation varies greatly from smoker to smoker, so that 10-80% of the condensate may be retained in the lungs, resulting in a range of 0.9-35 mg for the amount of smoke condensate retained in the respiratory tract per cigarette. The number of cigarettes smoked by an individual in epidemiological studies is therefore of no value without information as to his smoking habits.

63-1080 ACUTE LEUKEMIA AND CONSTITUTION. (Ger.) Panoff, A. (Child. Clin., Dist. Hosp., Sofia, Bulgaria). *Arch. Kinderheilk.* 168(2): 201-205, 1963.

A number of observations of abnormalities in the physical habitus of a series of six children of preschool age suffering from acute leukemia, particularly excessive piliation, is interpreted as indicating a dysfunction of the pituitary-adrenal system which results in an excessive production of androgens coupled with a decreased production of glucocorticoids. The latter may render the child less resistant against exogenous factors leading to the development of leukemia.

63-1081 THE INFLUENCE OF LINOLEIC ACID UPON THE GROWTH OF TRANSPLANTED SARCOMA. (E.) Sueyoshi, Y. (Dept. Biochem., Keio U. Sch. Med., Tokyo) and Y. Nagao. *Keio J. Med.* 11(4):223-225, 1962.

Rats which had been maintained on a fat-free diet for 3 wk. prior to the implantation of Fujinawa strain sarcoma developed the tumor much faster (all dead within 16 days) and of much larger size (824 mm² compared to 329 mm²) when after implantation they were fed with a normal diet for two wk. rather than when the fat-free diet was continued in the post-implantation period. If rats which had been maintained on the fat free diet following implantation were then fed with linseed oil or linoleic acid, the growth of the tumor was increased sufficiently so that in 4 days it reached the size seen in animals fed the normal diet.

63-1082 INDUCTION OF MALFORMATIONS OF THE MAMMARY GLAND AND OF THE NIPPLE IN FETUSES BY ESTRADIOL INJECTION INTO THE PREGNANT RAT. (Fr.) Delost, P. (Lab. Anim. Physiol., Fac. Sci., U. Clermont-Ferrand, France), Ch. Jean and Cl. Jean. *J. Physiol. (Paris)* 55(2): 237-239, 1963.

Estradiol dipropionate (10 or 20 mg s.c. in oil) to 14-day pregnant rats caused malformation in 100% of 21-day fetuses of both sexes. Fetuses from mothers receiving 20 mg showed complete inhibition of nearly all the primitive mammary gland and increase in the mammary area, with keratinization and thickening of the nipple epithelium. Among fetuses from mothers inj. with 10 mg, 43/48 lacked mammary gland pairs, with 5 pairs (usually inguinal) present in rudimentary form. In 2 cases the nipple was absent, and in the remaining cases it was imperforated and showed simple hypertrophy, sometimes with epidermal invagination and coelomastia. Fetuses from mothers receiving a 1 mg dose showed, in females, 75% total and 25% partial mammary gland inhibition and in males, 54% total and 25% partial inhibition and also 4.2% subnormal glands, 8.4% coelomastia, and 8.4% replacement of gland by epithelial cords.

63-1083 UNCONTROLLED GROWTH OF CELL POPULATION. (E.) Stewart, H. L. (NCI, Bethesda). *Milit. Med.* 128(7):610-612, 1963.

Recent findings dealing with the mode of action of some polycyclic hydrocarbons (benzo(e)pyrene, N-2-fluorenylacamide) tend to disprove the principle of direct action between a carcinogen and its target tissue. Instead, it appears that some carcinogens operate most effectively, or only, by an indirect mechanism. Other evidence of a complex mode of action is provided by result of tumor induction by viruses and physical agents where introduction by almost any route leads to cancers of more than 1 site. An interplay of complicated physiologic mechanisms including toxic and carcinogenic effects and leading to associated atrophy, nutritional and metabolic disturbances and specific tumor localizations appears to be operative in N,N'-2,7-fluorenyleneb-2,2,2-trifluoroacetamide and in N,N'-2,7-fluorenylenebisacetamide carcinogenesis. These same changes have been postulated by Crile in his "signal substance" theory of gastric carcinogenesis in humans with pernicious anemia and achlorhydria.

63-1084 BIOLOGIC AND HISTOLOGIC CHARACTERISTICS OF A MOUSE ASCITES-TUMOR INDUCED BY ISONICOTINIC ACID HYDRAZIDE. (Ger., Abstract) Juhász, J. and B. Szende. *Zbl. Allg. Path.* 104(5-6):315, 1963.

A new ascites tumor was developed in white mice by inoc. of ascitic fluid drawn from mice bearing isoniazid-induced reticulum cell sarcomas of the mesenteric lymph nodes. Survival time among animals bearing the new tumor averaged 19-20 days; eventual tumor wt. approximated 50-70% of the animal's initial body wt. The rate of growth is directly proportional to the number of viable cells inoc.; the number of viable cells is maximal at 10-12 days (560 x 10⁶), with an increasing incidence of necrotic cells thereafter. The av. diameter of tumor-cell nuclei ranged from 8-22 μ . Active mitosis reached a peak at day 2, while

otic division figures began to increase after 12. Tumor takes were 100% during 42 uninterrupted passages to the time of report.

1085 DRUGS AND CONGENITAL ABNORMALITIES.

(E.) Hagen, E. O. (Dept. Anat., U. Alberta, Canada). Lancet 1:501, 1963.

aps of 12 female C57 Black and Strong A mice (about 10-weeks-old) were given thalidomide (50 mg/kg/day i.p.). They were then mated with appropriate males. The number of apparently viable fetuses at term in the A and C57 groups was 23 and 40, resp.; in controls given only the solvent (polyethylene glycol), 53 and 42, resp. Deformed fetuses were found. It appears that thalidomide differentially affects the strain A, probably causing fetal death by deforming them, while the resorbing fetuses varied in size.

1086 THE ETIOLOGIC ROLE OF LIVER DAMAGE IN CANCERS OF THE PROSTATE. (Ger.)

droi, Z. (Urol. Clin., Med. U. Budapest, Hungary). Urol. Int. 15(5):318-323, 1963.

plementing a review of the literature, the author reports a comparative study of 3 groups of subjects whose histories did not suggest liver disease or any metabolic dysfunction. Tabulated data: av. age, number of cases, and percentage of bilirubin, thymol, transaminase, and sulphalein, resp., as follows: normal controls - 59, 23, 0, 5, 15.7, and 41.9; pts. with untreated prostatic cancers - 62, 26, 7.7, 11.1, 15, and 64.4; pts. under estrogen therapy for prostatic cancers - 60, 17, 5.8, 23.5, 25, and 15. He concludes that hepatic dysfunction and resulting secondary hormonal dysfunction, is one of the etiologic factors in development of prostatic malignancy.

1087 CYSTS OF THE EPIDIDYMISS, CANCER OF THE CERVIX, GRANULAR CELL MYOBLASTOMA, AND OTHER LESIONS AFTER ESTROGEN INJECTION IN SPERM MICE. (E.)

Dunn, T. B. (NCI, Bethesda) and A. W. Green. J. Nat. Cancer Inst. 31(2): 145-155, 1963.

and female mice from a noninbred Swiss strain and from inbred strains BALB/c and C3Hf (without the milk agent) received s.c. inj. of diethylstilbestrol (0.1 ml, 2% in saline, 100 µg) on the day of birth and a control group received the saline alone. Autopsy 13-26 mo. revealed lesions of the epididymis in over 90% of the male mice (14/23); female mice showed histologic evidence of continuous estrogen stimulation, concretions of the vaginal cavity (12/30 at 13 mo.), uterine cervical and vaginal cancer (1/30), granular cell myoblastoma of the uterine cervix (2/31). Among control rats, one C3Hf female, age 26 mo., had a granulosa cell tumor of the ovary (indicating continuous estrogen

stimulation) and a granular cell myoblastoma beneath the epithelium of the uterine cervix. It is suggested that prenatal and postnatal evidence (especially of intense estrogen stimulation in the female) be studied in relation to the etiology of human cancer.

63-1088 A STOCHASTIC MODEL OF CARCINOGENESIS COMPARED WITH MOUSE SKIN TUMOUR ENHANCEMENT

AFTER GASTRIC INSTILLATION OF 9,10-DIMETHYL-1,2-BENZANTHRACENE WITH SUBSEQUENT LOCAL CONTINUOUS EXPOSURE TO "TWEEN 40". (E.) Niskanen, E. E. (Norsk Hydro's Inst. Cancer Res., Montebello, Norway) and N. Arley. Nature (London) 199:83-84, 1963.

The results of the original experiment (see CRA 1(2):#222, 1963) as to av. induction time versus dose and mean tumor incidence, are compared with those obtained using the stochastic model of carcinogenesis $\log(1-F) = -\beta(1-\exp[-\gamma c])$, where F is the theoretical mean tumor incidence, c the dose of carcinogen, and β and γ are estimated graphically from the experiment, (here β is 0.85 and γ is 2.12 mg^{-1}). Experimental and theoretical values for incidence and induction time are in good agreement, but experimental results for mean number of tumors/animal differed from those obtained by the model. This difference may be due to the fact that some tumors may have disappeared before being observable; also when there is more than 1 tumor/animal, they may not be of independent origin as assumed by the model. The author believes his experimental evidence supports the somatic mutation hypothesis of carcinogenesis as well as the view that carcinogens cause delayed maturation of the epidermal cells, and these, when exposed later to dipole type tumor enhancers (despite increased mitosis) may not lead to production of enough normally differentiating cells, the ultimate result of which is the formation of a focal epidermal tumor. (See also CRA 1(1):#20, 1963.)

63-1089 METABOLISM OF RADIOACTIVE METHYLCHOLANTHRENE IN THE RAT. (E.)

Goodall, A. L. (Roy. Infirm., Glasgow, Scotland), M. H. McIntyre and J. S. Kennedy. Nature (London) 198:1317-1318, 1963.

After admin. of 20-methylcholanthrene-6- C^{14} ($2.55 \text{ mC/}^{\mu\text{mM}}$, 10 mg, intragastric) to 6 female Sprague-Dawley rats from 2 separate colonies, after autoradiography, radioactivity after 1, 3, and 5 days was highest in the stomach (max. at cardiac end), high in kidney and was found in decreasing amounts in liver, large intestine, rectum and small intestine. After 8 and 14 days there was no significant radioactivity. No activity was found in other tissues examined; neither were there histological abnormalities including the mammary gland. Feces showed highest activity after 48 hr., which diminished to practically zero at 93 hr. The study suggests that the

carcinogen was absorbed by the stomach and intestines, metabolized in normal fashion by liver and kidneys and excreted in urine and feces.

- 63-1090 CARCINOGENICITY OF EPOXIDES, LACTONES, AND PEROXY COMPOUNDS. (E.) Van Duuren, B. L. (Inst. Indust. Med., New York U. Med. Ctr., New York), N. Nelson, L. Orris, E. D. Palmes and F. L. Schmitt. *J. Nat. Cancer Inst.* 31(1): 41-55, 1963.

Available information about the carcinogenicity of epoxides, lactones, hydroperoxides and peroxides is reviewed and 8 epoxides, 6 lactones and 1 hydroperoxide of known carcinogenic activity are listed and described. In addition, tumor responses were determined for 14 more compounds tested on male Swiss-Millerton mice by skin painting 3x/wk., 100 mg/painting. Results are compared using a malignant tumor index (M.I.) = 10000/days required to produce malignancy in 50% of the animals, adjusted by observed survivals. Among epoxides 5/8 were found to be carcinogenic: styrene oxide (in 10% benzene) and 1,2-epoxybutene-3 (a malignant index of <10, but 1/30 malignancies with each); 1-ethyleneoxy-3,4-epoxycyclohexane (in 10% benzene), dl-1,2,3,4-diepoxybutane (in 10% acetone), and the meso-form of the same, also in acetone, had malignant indices of 22, 16, and 23, resp. Of hydroperoxides, 1-hydroperoxy-1-vinylcyclohexene-3 (in 0.5% benzene-1-vinyl-cyclohexene-3 (1:1)) and 1-vinylcyclohexene-3 (in 50% benzene) had M.I. of 15 and 10, resp.; M.I. <10 were found in 2 peroxides and 2 lactones examined, but γ -butyrolactone did cause malignancy in 1/30 mice. A malignant index of 21-36 was obtained with mice painted with 3,4-benzpyrene, (100 ppm/acetone or in benzene), whereas acetone or benzene alone gave malignant indices of <10. Results suggest that strained lactone rings may favor carcinogenicity.

- 63-1091 THYROID ACTIVITY IN CARCINOGEN TREATED RATS. (E., Abstract) Newman, W. C. (Dept. Physiol., U. Tennessee, Memphis) and R. C. Moon. *Physiologist* 6(3):246, 1963.

In 50-day-old Sprague-Dawley female rats, given 20-methylcholanthrene (20-Me; 10 mg/day x 30, p.o., in sesame oil) thyroid activity (TSR), compared to controls treated with sesame oil, was decreased approx. 25% during treatment as compared to TSR prior to treatment with 20-Me. Average TSR after 20-Me treatment was completed was comparable to TSR rate before treatment. Thyroidal 131 I was fed for 24 hr. prior to the following: daily intragastric feedings of 1 ml sesame oil for 3 days, then 10 daily feedings 10 mg 20-Me in sesame oil, 5-7 days. The av. hourly release of thyroidal 131 I was significantly less during 20-Me feeding when contrasted with controls given only sesame oil, indicating 20-Me depressed thyroid activity, which in turn may influence the rate of tumor induction by 20-Me.

- 63-1092 TRANSPLANTATION OF HOMOLOGOUS AND HETEROLOGOUS TUMORS. STUDIES OF SEROTONIN AS A CONDITIONING AGENT. (E.) Convalius, (Dept. Surg., Hahnemann Med. Coll., Philadelphia Pa.), J. M. Howard and J. G. Strawitz. *Arch. Su.* 86(3):480-483, 1963.

Rats implanted with the Walker 256 carcinosarcoma (1 ml/hr. x 7 of cell suspensions aged 1-7 hr. s.c.) from female Sherman rats had higher tumor takes (60-90%, depending on duration of aging) and a higher rate of tumor growth when conditioned with serotonin (0.4 mg/day x 7 i.m.) starting at the time of tumor inoc. A lower dose of serotonin (0.2 mg/day) failed to yield tumor takes in Wistar rats inoc. with the heterologous HEP III (human) tumor, although serotonin (0.4 mg/day x 4), cortisone (6 mg/day x 3), X-irradiation (150 r) + serotonin (0.2 mg/day x 4) and X-irradiation + cortisone produced tumor takes of 40% of 20, 60% of 30, 77% of 99 and 90% of 106, resp. In these groups of conditioned animals the av. tumor wt. was 6.0-7.3 g; in untreated controls or irradiated (150 r) rats tumor takes did not exceed 20%, and tumor growth was poor.

- 63-1093 ON A TREATMENT OF TOBACCO INTENDED TO REDUCE POLYCYCLIC HYDROCARBON CONTENT CIGARETTE SMOKE. (Fr.) Waltz, P. (Fabriques de Tabac Reunis S. A., Neuchatel-Serrieres, Switzerland) and M. Häusermann. *Zschr. Praeventivmed.* 8(2):111-124, 1963.

Cut Maryland tobacco, pretreated with methylene chloride which removed 2.8% of the extractable material (including 0.51% paraffins), when made into cigarettes and smoke mechanically, yielded 24.0 mg of crude smoke condensate per cigarette; 3,4-benzpyrene (BP) content per 100 cigarettes and per 100 g of tobacco was 1.52 and 2.03 μ g, resp. Control cigarettes made from similar but nontreated tobacco produced 28.8 mg smoke condensate, containing 1.67 and 2.23 μ g of BP, resp. However, while the extraction treatment reduced the smoke condensate by 16.7% and the BP by 9%, the conc. of BP in the condensate was increased (treated 0.64 ppm, control 0.58 ppm). Thus the method of tobacco extraction by pretreatment with methylene chloride does not produce a specific reduction of BP in the smoke. The decreases obtained are considered insignificant, being comparable to the effect of a poor filter. (See also CRA 1(5):#868, *ibid.*, (6):#1094, and #1095, 1963.)

- 63-1094 EXAMINATION OF A PROCEDURE FOR THE TREATMENT OF TOBACCO BY PRIOR EXTRACTION (CONDENSED FROM THE MINUTES OF CORESTA). (Fr., Abstract) Ctr. Coop. Sci. Res. Tobacco (CORESTA), Paris. *Zschr. Praeventivmed.* 8(2): 138-140, 1963.

A reevaluation of the Neukomm-Bonnet patented process for removal of polyaromatic hydrocarbons from tobacco through pre-extraction with carbon

chloride or other chlorinated solvents formed the negative results obtained in 1961. Experiments by Waltz and Häusermann designed to investigate two possible reasons for failure of the patented process (a) failure of the pressure machine to extract the compounds, or (b) extraction may be achieved only from "black" residues gave negative results. A third possibility, that the procedure used to collect smoke was invalid, was also shown to be incorrect. Thus the original conclusions of the report remain in force. (See also CRA #1093, 1963.)

95 STATISTICAL REMARKS ON THE EXPERIMENTS OF J. L. NICOD CONCERNING THE CARCINOGENIC EFFECT OF PRE-EXTRACTED TOBACCO.

(Fr.) Uhlmann, W. (Inst. Related Math., Tech. Sch., Braunschweig, Germany). Zschr. Entw. Med. 8(2):140-144, 1963.

Studies of J. L. Nicod on the carcinogenic effect of treated (pre-extracted) and untreated tobacco on mice were criticized from the statistical point of view. If from the original group of mice (5 groups of 40 each) are deleted animals not counted because they (1) died accidentally, (2) apparently died "too early" and were not counted, (4) were in too poor condition to be used, the remainder totals 141 (including 1 that was apparently added to the treated tobacco group). The experiments seemed to indicate that the incidence of cancer cases was higher in the treated tobacco group (Orient and American = 4/34) than in the untreated groups (Orient = 7/17, 3/7 in an early group and American = 9/39, 2/9 in an early group). However, adequate statistical tests of the reliability of the difference in cancer incidence were not carried out by Nicod. To statistically verify the difference, χ^2 should be 84 (95% reliability). In the experiments of Nicod, χ^2 was 2.178 for Orient and 1.566 for American tobacco; if the 2 groups were combined only 3.192. It was concluded that only statistical tests could determine the effects of treatment of tobacco. (See also CRA 1(6):1093, 1963.)

96 DELAYED CARCINOMA INDUCED BY BERYLLIUM AEROSOL IN MAN. (Ger.) Niemöller, H. Int. Arch. Gewerbepath. 20(2):180-186, 1963.

The first of 2 cases with delayed lung carcinoma, regular exposure to beryllium lasted 15 yr. Lung damage was observed 3 yr. after X-ray examination. The pt. died 16 yr. after the last exposure (following surgery). Autopsy included a carcinoma in scar tissue, secondary tumors in the hilar lymph nodes, adrenal gland and cerebellum. While beryllium granuloma could not be found, beryllium residues were detected in the lung tissue.

The second case followed a similar pattern, with the mediastinal carcinoma being detected again 16 yr. after last exposure, but this time following a progressive berylliosis. A third pt. is mentioned as presenting radiological evidence of a similarly located stationary tumor. In reference to the increasing incidence of lung cancer, it is felt that investigation of the possible contributory role of the beryllium present in cigarettes is justified.

63-1097 VASCULAR CHANGES DURING EXPERIMENTAL CARCINOGENESIS OF THE CHEEK POUCH OF THE GOLDEN HAMSTER. (Fr.) Delarue, J. (Lab. Pathol. Anat., Paris), J. Mignot and T. Caulet. C. R. Soc. Biol. (Paris) 157(2):222-225, 1963.

Topical application of 9,10-dimethyl-1,2-benzanthracene to the cheek pouch of the golden hamster, (0.5% in liquid petrolatum 3x/wk. for 3 mo.) induced either nonmalignant papillomas or vegetating carcinomatous tumors (epitheliomas), preceded in both cases by a long period of vascular dilatation. In precancerous lesions only, this was accompanied by marked modifications of the capillary reticular pattern (abrupt changes of direction of flow, irregularity in the size, and frequent, localized areas of ectasia).

63-1098 TWO CASES OF BENZENE-INDUCED ACUTE LEUKEMIA. (Fr.) Larcen, A., C. Pernot and F. Streiff. Arch. Mal. Prof. 24(6):559-561, 1963.

In a group of 20 men who worked in the same room and were subjected to periodic inhalation of benzene vapors from containers of varnish and insulating compound, there developed one case of acute, paramyeloblastic leukemia and one of pre-leukemic leukosarcomatosis; length of exposure was approx. 2 yr. Although the authors attribute both illnesses to such inhalation, on grounds of statistical probability, they also point out that the father of the pt. with leukosarcomatosis died of the same disorder 2 yr. after the death of his son, in the absence of any known exposure to carcinogens. It is emphasized that a carcinogen may induce, in different individuals, different disorders, such as leukemia or aplastic anemia.

63-1099 INFLUENCE OF 3-METHYLCHOLANTHRENE ON PITUITARY LACTOGEN CONCENTRATION. (E., Abstract) Moon, R. C. (Dept. Physiol., U. Tennessee Med. Units, Memphis). Fed. Proc. 22(2):314, 1963.

A single feeding of 20-methylcholanthrene (20-Me; 10 mg intragastrically) to lactating rats separated from their litters on day 14 of lactation resulted in an initial lowering of pituitary lactogen, followed by a rebound to control levels at 24 hr. postfeeding. A max. lactogen depletion

of 45% was evident at 16 hr. postfeeding. Pituitary lactogen content in rats receiving 30 mg 20-Me was about 50% below control levels at 24 hr. The data suggest that 20-Me is capable of providing a hormonal state conducive to mammary tumor growth in the rat, in addition to its more direct carcinogenic effect on mammary cells.

63-1100 INDUCTION OF TUMORS IN GERMFREE RODENTS BY METHYLCHOLANTHRENE. (E., Abstract) Pollard, M. (Lobund Lab., U. Notre Dame, Notre Dame, Indiana). Fed. Proc. 22(2):314, 1963.

20-Methylcholanthrene (20-Me; in oil) was inj. s.c. into germfree newborn or adult Swiss Webster mice or Fischer rats. All mice developed lung adenomas at 8 wk. in those inj. at birth; and later, s.c. fibrosarcomas when inj. as adults. The latter tumors were transplantable through 5 series of Swiss Webster mice. Within 7 mo. after 20-Me inj. all adult germfree rats developed sarcomas, whereas only 56% of those raised under conventional conditions had tumors. The tumors of germfree animals were indistinguishable histologically from those of conventional animals. All attempts at demonstration of a viral agent in germfree animals have so far been negative, including serology, skin tests, inoc. of tissue and fecal extracts into germfree tissues, examination of tissue cultures prepared from tumor tissues, and electron microscopic examination of the tumors. (See also CRA 1(1):#59, 1963.)

63-1101 GROWTH OF CULTURED HUMAN TUMOR CELLS IN CONDITIONED ANIMALS. (E.) Koike, A. (2nd Dept. Surg., Nagoya U. Sch. Med., Japan). Nagoya J. Med. Sci. 25(2):99-105, 1963.

Cells from 6 cultured lines (originally from human tumors, 3 carcinomas, 2 sarcomas, 1 mesothelioma) were inoc. s.c. into the thighs of cortisone-conditioned irradiated weanling Long-Evans rats or into LAF1 mice bearing the ACTH-secreting tumor At-T 20 (carried in LAF1 mice). In conditioned rats and ACTH-secreting tumor-bearing mice, resp., tumor take from 10⁶-10⁷ tumor cells of various lines were: # 191, 65% of 17 and 72% of 18; # 212, 78% of 18 and 60% of 10; # 41, 83% of 29 and 80% of 15; # 131, 40% of 20 and 94% of 18; and # 1922 and # 1938 into cortisone-conditioned animals only, 79% of 14 and 72% of 14. Only 1 of the tumors growing in conditioned rats (# 41 arising from an osteogenic sarcoma) was transplantable; in 3 passages in the same conditioned rats, there was development of some lung metastases. The tumors growing in mice maintained a structure resembling that of the original tumors, and showed less necrosis and fibrosis. One cell line (#131 arising from an ovarian carcinoma) grew better in ovariectomized mice (mean tumor wt. 0.39 g), than in intact or estrogen-treated ovariectomized mice (0.24 and 0.05 g, resp.). Acquired tolerance could not be obtained

when newborn or fetal mice were inj. i.v. with several of the tumor cell lines or with human lymphocytes.

63-1102 CORPUS CARCINOMA DEVELOPING IN A PATIENT WITH TURNER'S SYNDROME TREATED WITH ESTROGEN. (E.) Dowsett, J. W. Am. J. Obstet. Gynec. 86(5):622-625, 1963.

A pt., age 22, with an adenocarcinoma of the cervix of endometrial origin had received during the preceding 6 yr. 5845 mg of diethylstilbestrol (DES; from 1-5 mg/day) for Turner's syndrome. When first seen at age 16 the pt. had castration levels of urinary gonadotropin, and a buccal smear revealed a genetic male. During DES treatment there were several episodes of withdrawal bleeding, the last of which could not be controlled by discontinuation or by large doses of progesterone. The pt. was clinically well 4 yr. after radical hysterectomy and irradiation.

63-1103 INDUCTION OF SARCOMA IN THE RAT BY CADMIUM SULPHIDE PIGMENT. (E.) Kazantzis, G. (Med. Res. Coun. Air Pollution Res. Unit., St. Bartholomew's Hosp. Med. Coll., London). Nature (London) 198(1):1213-1214, 1963.

After admin. of CdS (25 mg, equivalent to 20 mg of metallic Cd, x 2 inj. s.c. to 2 different sites on a single occasion) to ten 6-month-old female Chester Beatty strain rats, a small, hard, mobile nodule developed at each inj. site without evidence of an inflammatory reaction in the overlying skin. In the following 6-10 mo. nodules grew and produced highly cellular sarcomas of fibroblastic origin at one of the two inj. sites in 5/10 and at both inj. sites in 1/10. The remaining 4 died during this period without having developed tumors.

63-1104 EFFECT OF CASTRATION ON INDUCTION OF PITUITARY TUMORS WITH DIETHYLSTILBESTROL IN THE SYRIAN HAMSTER. (E., Abstract) Russfield, A. B. (Child. Cancer Res. Foundation Boston, Mass.) Proc. Am. Assn. Cancer Res. 4(1):59, 1963.

In a group of male syrian castrated hamsters (number unspecified) surviving 8 mo. after implantation of diethylstilbestrol (DES; 15 mg pellets s.c. repeated at 4 mo. intervals) 6 developed pituitary tumors, all of the intermediate lobe type, av. wt. 34.5 mg. In an equal group of DES-treated intact hamsters, 6 developed pituitary tumors (5/6 chromophobe adenomas with marked intermediate lobe hyperplasia, 1/6 intermediate lobe type); av. wt. was 53.9 mg. All animals bearing chromophobe adenomas had adrenal changes suggesting early neoplasia, but no evidence of mammary gland stimulation. It is suggested that histological differences seen in estrogen-induced pituitary tumors in castrate and intact hamsters may be linked with differences

in the adrenals, and specifically with same factors causing the inhibition of spontaneous adrenal carcinogenesis in castrated hamsters.

05 NEW HETEROAROMATIC COMPOUNDS. XVIII. BORON-CONTAINING ANALOGS OF BENZ(a)ANTHRENE. (E.) Dewar, M. J. S. (George Herbert Lab., U. Chicago) and W. H. Poesche. Chem. Soc. 85(15):2253-2256, 1963.

esis of a series of derivatives of 5,6-dimethyl-5-borazarobenz(a)anthracenes is described with the hope that they may possess carcinogenic or anticarcinogenic properties.

06 INCREASE OF INDUCED SKIN TUMORS IN THE MOUSE BY THE LETHAL YELLOW GENE. (E.) Vlahakis, G. (NCI, Bethesda) and Heston. J. Nat. Cancer Inst. 31(1):189-195,

inbred Swiss females SWR homozygous for (AA) were crossed with highly inbred YBR, heterozygous for the lethal yellow (AYa) to give F1 progeny AYA (yellow), (agouti). On skin painting with methylcholanthrene (0.1 ml of 0.25% soln. in benzene x 12) the frequency of skin tumors and spontaneous sarcomas for AYA males and females, was 44/49 (89.8%) and 49/50 (98%) for sarcomas, 47/49 (95.9%) and 49/50 (98%) for epidermoid carcinomas, 3/49 and 0/50 for basal carcinomas, and 2/49 and 0/49 for s.c. carcinomas. For the combined sexes average lag in first painting and first papilloma was 1.1 wk., and average time between first papilloma and death was 7.9 wk. For males and females without the AY lethal gene (AaF1 hybrids) frequencies were 41/50 (82.0%) and 46/52 (88.5%) for papillomas, 44/50 (88.0%) and 48/52 (92.3%) for epidermoid carcinoma, 0/50 and 2/52 for basal cell carcinoma, and 6/50 and 0/52 for sarcoma. Average lag in papilloma formation was 14.9 wk., and mean time between papilloma appearance and death was 9.1 wk. While all differences were in the same direction, suggesting that presence of the AY gene increases susceptibility to the induced tumors, none were statistically significant possibly due to the low frequency of tumors in the 2 groups.

7 THE "MELANO-SEBACEOUS BODY" OF THE GOLDEN HAMSTER. III. REACTION TO SHORT-TERM LOCAL APPLICATION OF VARIOUS CARCINOGENIC CHEMICAL COMPOUNDS. (Fr.) Oberman, B. (Exp. Med., Inst. Sci. Res. Cancer, St. Germain (Seine), France) and M. R. Rivière. Ass. Franc. Cancer 49(3):331-339, 1962.

hamsters (*Mesocricetus auratus*) age 2-4 were painted for up to 40 days in the region of the "flank organ" with 1% solutions (in oil) of 0-dimethyl-1,2-benzanthracene (DMBA), 3,4-

benzpyrene (BP), or 20-methylcholanthrene (20-Me). Only those treated with DMBA showed progressive wt. loss approaching cachexia by day 40. All 3 compounds caused progressive hyperplasia of the epidermis, with concomitant atrophy and decrease in number of the sebaceous components of the organ. The changes were marked in DMBA-treated, less pronounced in BP- and slight in 20-Me-treated hamsters. The melanocyte components of the organ remained essentially unchanged.

63-1108 INFLUENCE OF HEREDITY ON SPONTANEOUS AND INDUCED LUNG CARCINOGENESIS IN THE MOUSE. (Fr.) Rudali, G. (Lab. Genet., Radium Inst., Paris), N. Yourkovski and L. Juliard. Bull. Ass. Franc. Cancer 49(3):270-277, 1962.

Analysis of 5 pure mouse strains for spontaneous lung cancers (all adenomas) gave the following incidence (in 10 mo. survivors) and mean survival for tumor-bearing mice: A/He 23%, 380 days; XVII/G 19%, 563 days; NLC 2%, 450 days; none occurred in 87 male RIII or in 924 C57BL mice. In line XVII/G no mammary cancers or leukemias have been observed in over 11 yr.; the NLC line is known to carry the Bittner mammary tumor agent (MTA); the C57BL line has a spontaneous incidence of lymphatic leukemias of 1.5-1.8%. On admin. of urethan (U) 1×10^{-3} or 1×10^{-4} , resp. (in tap water, *ad lib* starting at 2 mo.) the following frequencies of lung tumors were found at 6 mo.: A/He 100% of 14 and 100% of 10; XVII/G 100% of 14 and 100% of 20; NLC 100% of 16 and 73% of 19; RIII 92% of 24 and 21% of 29. All tumor-bearing animals presented 5-20 tumors. In the C57BL line the frequency of lung adenomas at the high and low U doses was 57% of 14 and 6% of 34, with 1-2 tumors/tumor-bearing mouse. Consumption of U varied between strains, ranging from 2.2-4.1 ml/day, but was highest with the C57BL strain, lowest with strain RIII. Toxicity was observed at both doses, with 194/250 surviving 6 mo. F1 hybrids from reciprocal crosses of the C57BL x XVII/G lines treated with U (1×10^{-3}) had 100% frequencies of lung adenomas (with 2/59 showing in addition leukemias), suggesting that the resistance is due to a genetic rather than a viral factor. This hypothesis was supported by studies of tumor induction in newborn C57BL and XVII/G mice (nursed for 35 days by mothers receiving 20-methylcholanthrene, 0.1 ml of 0.5% soln./day by gavage, in arachis oil x 20 days of pregnancy, to a total of 10 mg). Of 40 XVII/G F1 mice, 17 survived 115 days, and 100% of these developed lung adenomas, surviving a mean of 232 days. Of 91 C57BL F1 mice, 40 survived 240 days, and none of these developed lung adenomas, although 1 had lymphatic leukemia.

63-1109 HYPERPLASTIC ALVEOLAR NODULES IN THE MAMMARY GLAND OF HYBRID MICE, A/Jax AND AKR CROSS, THAT RECEIVED ESTROGEN ADMINISTRATION OR WHOLE-BODY X-RAY IRRADIATION. (E.) Nishizuka, Y. (Dept. Path., Mie Prefectural U. Sch. Med., Tsu, Japan), T. Sakakura and H. Miyawaki. Mie Med. J. 12(1):77-93, 1962.

After estradiol benzoate (E; 20 μ g/wk. x 20, s.c.) beginning at 30-41 days of age, incidence of mammary cancer in (A/Jax females x AKR males) F₁ hybrid virgin females was 52.6% at an av. age of 514 days (11 mo. after discontinuation of E). In irradiated mice (150 r/wk. x 4, beginning at 33-44 days) incidence was 8.3% at 239 days (7% in 592 days in virgin controls). In 24 irradiated mice, 16 developed lymphosarcomas and 11 ovarian tumors (7 of these had concurrent lymphomas). None of the irradiated mice with mammary cancers had other tumors. Among 9 E-treated mice, 5 developed leukemia and none ovarian tumors; among 69 controls there were 13 lymphosarcomas and 1 ovarian tumor (11 of these 13 were among 45 which had received s.c. transplants of thymus and spleen from AKR males at approx. 40 days). The av. number of hyperplastic alveolar nodules/gland in E-treated mice was 17.38. In irradiated mice mean nodule response was reported for 3 subgroups: 8.37 for 6 with hormone-secreting ovarian tumors; 0.68 for 5 with trabecular ovarian tumors; and 0.13 for 3 with immature glands (controls, 2.01). The mammary glands of E-treated mice were characterized by profuse lobulo-acinar development and dilated ducts filled with secretion; irradiated mice with hormone producing ovarian tumors exhibited similar development except for fewer number of nodules; irradiated mice with non-hormone secreting trabecular ovarian tumors or no ovarian tumors showed mammary gland involution and a low incidence of nodules indicating castration following irradiation. The authors postulate that irradiation caused castration and mammary gland involution. Subsequently, in response to stimulation by hormone secreting ovarian tumors, some animals show gland development resembling that of E-treated mice, but did not have enough time to develop cancer. It is also suggested that the development of cancers from nodules is a process consisting of a sequence of events requiring a certain period of time; and that once the gland has regressed, it has lost the capacity to develop cancer from nodules.

63-1110 ROLE OF THE DRAINING LYMPH NODE IN CHEMICAL CARCINOGENESIS. (E.)

Anderson, M. R. (Algernon Firth Inst. Path., Sch. Med., Leeds, England). *Nature (London)* 198:599-600, 1963.

Temporary suppression of the activity of the lymph nodes draining the site of 20-methylcholanthrene (20-Me; 0.05 g s.c. in the anterior abdominal wall) inj. (a) by prior inj. of Thorotrast (0.05 ml) directly into the superficial, inguinal, epigastric and axillary lymph nodes or (b) by single dose local irradiation of the inguinal, epigastric and axillary lymph nodes with 2000 r (2 days before 20-Me), delayed the onset of cancer by 6-7 wk. At 26 wk. the frequency of tumor induction was 53% in Thorotrast injected, 58% in X-irradiated and 76-77% in control animals. Results suggest that the

process of chemical carcinogenesis may be in part mediated by an immune reaction originating in the regional lymph nodes about the area of carcinogen application, possibly a cell bound antibody.

63-1111 ELECTIVE PRODUCTION OF PHOCOMELIA BY NITROGEN MUSTARD. (Fr.) Salzgeber (Lab. Exp. Embryol., Coll. France, Paris). *J. Embryol. Exp. Morph.* 11(2):413-429, 1963.

Additional details are given of the paper abstracted in CRA 1(2):#216, 1963. The range of concentrations of nitrogen mustard employed was 0.6-1.6 μ g/egg. After treatment with 0.6- μ g, of those embryos that could be evaluated, deformities were seen in 1/1 treated in stage 43/47 treated in stage 18-19, and 116/130 treated in stage 20-22. After 1.2-1.6 μ g, 21/21 treated at stage 20-22 were deformed.

63-1112 ISONIAZID AND PULMONARY TUMORS IN MICE. (E., Abstract) Weinstein, H. J. (Duarte, Calif.) and R. Kinoshita. *Am. Rev. Resp. Dis.* 88(1):124-125, 1963.

Female Strain A mice (high spontaneous incidence) and C57 black mice (low spontaneous incidence) 4-6 wk. old were fed isoniazid which had been incorporated into food pellets at various concentrations (0.025% to 2%). Other groups received daily i.p. inj. of 2.5 mg or 10 mg/kg. After 32 wk. a significant number of pulmonary adenomas developed in Strain A, which appeared to be dose-related. The C57 findings were similar, but the observed lesions were difficult to classify and could have been either neoplastic or proliferative responses to intense inflammation. Metastases were not found in any of the animals. It was concluded on the basis of results in Strain A that isoniazid has tumor-inducing or accelerating capacity in mice.

63-1113 SELECTIVE DESTRUCTION IN TESTIS INDUCED BY 7,12-DIMETHYLBENZ[a]-ANTHRACENE. (E.) Ford, E. (Ben May Lab. Cancer Res., U. Chicago, Ill.) and C. Huggins. *J. Exp. Med.* 118(1):27-40, 1963.

After a single feeding (20 mg) or i.v. inj. (0.1-5.0 mg) of 9,10-dimethyl-1,2-benzanthracene the testes of rats were severely and selectively damaged, whereas the ovaries of sister rats were not damaged. Eventually, complete recovery of the testis occurred. This testicular effect was not seen with 20-methylcholanthrene (5.0 mg i.v. or 105 mg p.o.), 3,4-benzpyrene (5.0 mg i.v. or 100 mg p.o.), or 2-acetoaminophenanthrene (4 mg p.o.). The primary sites of destruction were the spermatogonia and resting spermatocytes. Initially, a severe atrophy occurred, secondary to destruction of precursors in the seminiferous cell line. Interstitial cells were not destroyed. Estimation of malic dehydrogenase (MDH) was

to determine the extent of damage to the tubular cells. The MDH level varied inversely in relation to testicular wt. No further development was reported during periods of observation up to 140 days.

114 CONTACT REACTIVITY TO CARCINOGENIC POLYCYCLIC HYDROCARBONS. (E.) Old, J. (Sloan-Kettering Inst., New York), Benacerraf, and E. Carswell. Nature (London) 196:1215-1216, 1963.

Female Hartley strain guinea pigs immunized with total doses of 250 µg of various polycyclic hydrocarbons in acetone were tested for contact sensitivity after 2-3 wk. and graded from +3 to negative (-) according to degree of induration and erythema at the site. When 20-methylcholanthrene (20-Me) was the sensitizing agent, the degree of contact reactivity to fixed conc. of 1%, 0.1%, 0.01% and 0.001% solutions with 20-Me was +3, +2, +1, and -, resp.; with benzpyrene (BP), +3, +2, +1, and -, resp.; with 9,10-dimethyl-1,2-benzanthracene (DMBA), +3, +2, +1, and -, resp. When BP was the sensitizing agent, the degree of contact reactivity with 20-Me was +1, +, -, -, resp.; with BP, +3, +2, +1, and -, resp.; with DMBA, +3, +2, +1, and -, resp. With DMBA as the sensitizing agent, results were, with 20-Me, +3, +2, +1, and -, resp.; with BP, +2, +, -, -, resp.; with DMBA, +3, +2, +1, and -, resp. The absence of cross reactivity suggests that homologous areas of the molecule are involved in conjugation to host protein although some may be due to impurity. Anthracene and phenanthrene were not found to be reactive. The degree of delayed sensitivity may be related to the high degree of resistance to chemical carcinogenesis in the guinea pig; they show poor or questionable contact sensitivity and are highly susceptible to chemical carcinogenesis.

15 EFFECTS OF ALCOHOL IN MOUSE NEOPLASIA. (E.) Ketcham, A. S. (NCI, Bethesda),

H. Wexler and N. Mantel. Cancer Res. 23(5): 667-670, 1963.

Mice (CDBA/2F1 females) given 20% alcohol (by volume in their water) survived indefinitely but showed marked but reversible changes in the appearance of liver fat. Over a period of 15 mo. on the alcohol no evidence of tumorigenesis was found. The regimen did not alter the growth or stimulate the metastatic spread of a transplanted tumor (Cloudman S-91), nor did it interfere with the reduction in metastatic spread due to surgical removal of the tumor. It is concluded that if alcohol plays a role in mouse neoplasia, it is one dependent on factors missing from the current experiments.

63-1116 A REASSESSMENT OF THE THYROID TUMORS INDUCED BY GOITROGENS IN MICE. (E.)

Bielschowsky, F. (Hugh Adam Dept. Cancer Res., U. Otago, Dunedin, N. Zealand) and C. M. Goodall. Proc. Univ. Otago Med. Sch. 41(1):3-5, 1963.

Three groups of female NZO/B1 mice were given 0.05% methylthiouracil in their drinking water for 42 wk. Of 15 mice killed after this treatment, 10 had thyroid tissue in their lungs, with invasion of surrounding tissues (especially veins). One mouse had a large spindle cell carcinoma of the thyroid with massive pulmonary metastases. Among 14 given a previously described thyroid digest for an additional 20 wk., 7 had thyroid deposits in the lungs. Animals kept for 20 wk. without further treatment had enlarged nodular thyroids. Small areas of active-looking tissue alternated with colloid-rich resting follicles. These same features were seen in 6 mice that were grafted with the whole thyroid from normal isologous donors 1 wk. after withdrawal of goitrogen. In two of the 14 mice treated with the thyroid digest the lesions apparently progressed independent of the initiating stimulus. However, in the 12 others of this group, the thyroid digest arrested growth of the gland and caused involution of both the gland and the pulmonary metastases.

See also abstract nos.: 1032, 1037, 1129, 1145, 1175

VIRAL CARCINOGENESIS

- 63-1117 **MUTAGENIC ACTIVITY OF A VIRUS IN HUMAN LEUKEMIA.** (Fr.) Torrioli, M. (Cancer Inst., Rome, Italy). *Acta Un. Int. Cancr.* 19(1-2):401-403, 1963.

Included in a review covering 20 yr. is a summary of the author's work which demonstrated in the blood of leukemic humans a filterable heat-labile agent which was capable of producing morphologic alterations when inoc. into fertilized chicken eggs. The agent causes a mesenchymal disease fatal to embryos by day 14 of incubation due to perivascular infiltration of mesenchymal cells, with signs of erythroblastic evolution in all organs; loss of normal hematopoietic activity of endothelium of vessels; and erythroblastic and leukoblastic infiltration of all embryonic organs. Mitotic alterations observed in the erythrocytes of embryos with this induced erythremia are described, and chromosome studies, still in progress, are reported indicating mutagenic action of the agent on the hemoblastic cell nucleus.

- 63-1118 **MODE OF ACTION OF THE LEUKEMOGENIC AGENT EXTRACTED FROM RADIATION-INDUCED LEUKEMIAS IN THE C57BL MOUSE.** (Fr.) Duplan, J. F. (Radium Inst., Paris). *Acta Un. Int. Cancr.* 19(1-2):393-396, 1963.

Male and female C57BL mice inj. at age 24 hr. with 0.05 ml of a leukemic extract (from X-ray-induced leukemias in homologous animals) developed leukemias in 37% of 43, with a mean survival time (MST) for leukemic animals of 566 days. Mice inj. at day 30 with the leukemic extract (0.1 ml/wk. x 3) developed leukemias in 50% of 16, with a MST of 481 days; frequency of spontaneous leukemias was 4% of 23 controls with MST of 457 days. Irradiation (175 r/wk. x 4) starting at age 45 days increased the frequency of leukemias to 73% of 23 mice, with a MST of 230 days. Pretreatment of irradiated mice with leukemic extracts (0.1 mg/wk. x 3 starting at age 30 days and ending 24 hr. before irradiation) increased the frequency to 81% of 16, with a MST of 235 days. Concurrent irradiation and extract inj. (starting 24 hr. after the 1st, and ending 24 hr. after the 3rd irradiation) increased the leukemias to 100% of 15 mice, with a MST of 250 days. No leukemias were observed in 17 mice inj. at birth with reticulosarcoma extract. Of animals inoc. s.c. with leukemic extracts in the right side, 2 developed primary lymphosarcomas of the right inguinal lymph node, which appeared at 176 and 182 days, resp.

- 63-1119 **STUDIES ON MURINE LEUKEMIA -- NUCLEIC ACIDS.** (E.) Rich. M. A. (Lab. Cancer Res., Albert Einstein Med. Ctr., Philadelphia, Pa.), J. Geldner, L. W. Johns, Jr., M. Kalocsy, P. Meyers, E. L. Rothstein, R. Siegler and

J. Gershon-Cohen. *Trans. N.Y. Acad. Sci.* 25(6):580-589, 1963.

The RNA content of Friend virus-infected Swiss mouse spleen was 8.7 mg RNA/g spleen as compared to 5.7 mg/g spleen in uninfected controls. The RNA base ratios were guanine, 16; cytosine, 15; uracil, 9.3 in infected spleens as compared with ratios in uninfected spleens of 12.5, 10.4 and 6.5, resp. Swiss mice inj. intrasplenically with an extract prepared by salt treatment of infected spleen developed what was essentially malignant lymphoma; 8/20 developed leukemia. Friend disease did not develop. Among 5 animals given heated extracts, none showed evidence of disease after 12 mo.; among i.p. saline controls, 1/31 developed leukemia. The lymphatic leukemia could be transferred by cell-free passage to Swiss, BALB/c, and C3H mice; female Swiss mice showed greater response to this agent than did males. Electron microscopic studies of spleen, thymus, and lymph nodes revealed particles characteristic of Friend virus as well as those of other murine leukemia. Tail-like projections, 22 m μ in diameter and 85-210 m μ in length were observed on many virus particles. (See also CRA 1(4):#719, 1963.)

- 63-1120 **SEARCH FOR A "THYMIC HORMONE" IN THE ETIOLOGY OF LYMPHOID LEUKEMIAS IN AKR MICE.** (Fr.) Rudali, G. (Radium Inst., Paris). *Acta Un. Int. Cancr.* 19(1-2):252-254, 1963.

In AkR mice thymectomy at 5 wk. reduced the frequency of spontaneous leukemia from 81% of 38 control mice to 12% (4/33) with mean survivals for the leukemic animals of 385 and 270 days, resp. Treatment of thymectomized AkR mice with a dried preparation of calf thymus (1 mg = 14.7 mg wet wt. 2x/wk. for 3 wk. then 3 mg 2x/wk; thymectomy at 35 days) did not reverse the inhibitory effect on leukemogenesis; the extract had no effect in intact mice. The frequency of leukemias was 12% in thymectomized, 8% in thymectomized + extract-treated, 77-86% in untreated and 81% in intact + extract-treated mice. In similar experiments with C57BL mice, frequency of leukemia in controls was 2.5%, after thymic extract treatment, 3.3%. Further, in mice rendered parabiotic a few days after thymectomy of one partner and then separated at age 200 days, the frequency of leukemia was 64% of 11 in the intact, and 9% in the thymectomized partners, with mean survivals of 215 and 213 days, resp. These results are against the hypothesis that a "thymic hormone" is active in leukemogenesis in mice.

- 63-1121 **SPECIFICITY OF RESISTANCE TO TUMOR CHALLENGE OF POLYOMA AND SV40 VIRUS-IMMUNE HAMSTERS.** (E.) Habel, K. (NIH, Bethesda) and B. E. Eddy. *Proc. Soc. Exp. Biol. Med.* 113:1-4, 1963.

Groups of adult Syrian hamsters were inoc. i.p.

ch 0.1 ml of either polyoma or SV40 standard virus. One mo. later the virus-immunized groups and normal controls were divided into 2 subgroups, one of which was challenged with viable polyoma tumor cells, the other with SV40 tumor cells. The sera of the polyoma-immunized hamsters had a polyoma HI antibody titer greater than 1:280, while the SV40 immune and control animals' sera were negative. In contrast, the SV40 immune animals had demonstrable neutralizing antibodies against SV40 virus in their sera. In challenge with tumor cells, each group showed a 100-fold resistance to the cell inoculum responding to the original virus injection, while at the same time remaining entirely susceptible to the tumor cells of the opposite group. Thus, SV40 can be added to the growing list of virus-induced tumors in which there is evidence for a cellular antigen or antigens foreign to the host.

1122 FURTHER CHARACTERIZATION OF THE FRIEND VIRUS DISEASE. (E.) Mirand, A. (Roswell Park Mem. Inst., Buffalo) and T. Grace, Jr. Acta Un. Int. Cancr. 19(1-2):355, 1963.

In intact mice, hematocrit dropped immediately after infection with Friend virus and reached a minimal level of 36% at about 3 days, then rose to a max. of 80% at about 3 wk. Increased hematocrit was paralleled by increased splenic size and was accompanied by alterations in circulating blood elements (increase in WBC and platelets, early appearance of erythroblasts, increased levels and reticulocyte counts but unchanged leukocyte counts). Splenectomy, 3 days before or 7 days after virus admin. prevented increases in hematocrit, Hb, reticulocytes, WBC and RBC; however, splenectomized mice which developed splenomegaly showed a WBC of 200,000 at 75 days. In splenectomy was performed 21 days post-infection, hematocrit, RBC and WBC declined, the first 2 returning to normal levels in 25 days; 55 days hematocrit showed a drop to 22%; reticulocytes to 3.1×10^6 , but WBC increased to 282,000, paralleling development of hepatomegaly. A relatively specific increase in Fe^{59} uptake by spleen occurred shortly after infection but before spleen enlargement. When a splenic filtrate from Friend virus-infected HA/ICR Swiss mice was given to newborn Sprague-Dawley rats, phatic leukemia occurred in 60.7% of 263 rats after an av. of 130 days, accompanied by increased WBC, and by decreased RBC and hematocrit, splenomegaly and by thymic lymphomas. When Fe^{59} -free filtrates of such rats were returned to Swiss mice, typical Friend leukemia and leukocytosis was obtained in 80% of 30 after an av. of 27 days.

1123 IN VITRO STUDIES ON POLYOMA VIRUS INFECTED POLYOMA TUMORS INDUCED IN MICE. (E.) Hellström, I. (Inst. Tumor Biol.,

Karolinska Inst. Sch. Med., Stockholm). Acta Un. Int. Cancr. 19(1-2):328-329, 1963.

Analysis of cytopathogenic effects (CPE) and release of virus hemagglutinin in tissue cultures of mouse embryo cells, polyoma virus-induced tumors, and other tumors revealed varying degrees of sensitivity to the CPE of polyoma virus (PV). A number of different lines from single cells isolated *in vitro* from a sarcoma and carried by serial transfer *in vivo* also differed in sensitivity: 1 clone was sensitive to infection with 0.06 HA units/0.2 ml, another was resistant to 51 HA units/0.2 ml. Normal embryonic cells were 10x more sensitive than PV-induced tumor cells; the most resistant tumor was a clone of Earle's cells (NCTC 929) which were resistant to infection with 205 HA units/0.2 ml. New karyotypes appeared from 3 PV-induced tumors after culmination of the CPE; the new clones were resistant to superinfection with PV during 5-8 transplant generations *in vivo* but then became sensitive. The resistant karyotype was found as a minority fraction in 4/6 sensitive tumors. There was no difference between the growth rate of sensitive and resistant lines of the same tumor. It is concluded that PV resistance is not analogous to the immunity of lysogenic bacteria. Resistance appears to be an epiphenomenon not associated with the malignant nature of cells. It was impossible to correlate the differences in capacity to adsorb PV with the degree of resistance against PV infection.

63-1124 THE EFFECTS OF ACTINOMYCIN D ON GROWTH OF ROUS SARCOMA VIRUS *IN VITRO*. (E.) Temin, H. M. (McArdle Mem. Lab., U. Wisconsin, Madison). Virology 20(4):577-582, 1963.

Pretreatment of secondary cultures of chick embryo fibroblasts with actinomycin D (0.1 or 10 μ g/ml) for 3-7 hr. prevented by 90% subsequent multiplication of Rous sarcoma virus (RSV; strain r36) although the inhibition due to the lower conc. was completely reversed on removal of cells to fresh media. The higher conc. had no effect on multiplication of Newcastle disease virus. The incomplete inhibition of RSV multiplication in actinomycin-treated cultures was not due to the appearance of resistant mutant cells, since surviving cells were subsequently inhibited in multiplication of RSV strain r36 or H3Cl when pretreated with lower actinomycin conc. Treatment of cells with actinomycin D (0.2 μ g/ml) 1 or 16 hr. after virus infection also resulted in inhibition of virus multiplication, but in this case the inhibition was not reversible on removal of cells to fresh media. The actinomycin conc. used in this study caused little or no inhibition of cell division of the fibroblasts and Rous sarcoma cells present in infected cultures, and had no effect on the assay for RSV infectivity.

63-1125 ON THE ONCOGENIC EFFECT PRODUCED IN RATS BY TISSUE CULTURE PREPARATIONS SUBJECTED

TO THE ACTION OF HUMAN MAMMARY GLAND CANCER TUMOR EXTRACTS. (E.) Deichman, G. I. (Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). *Biull. Eksp. Biol. Med. (Eng.)* 53(2):199-202, 1963.

When culture fluids from kidney cells of *Macacus rhesus* and *M. cynomolgus* in tissue culture infected with extracts from 2 human mammary tumors for 7-25 days were inj. i.p. into newborn (2-18 hr. after birth) nonpedigreed rats, after 11-20 mo. sarcomas developed in 18.7% of experimental rats and in 15.6% of control rats in direct contact with experimental animals. Tumors developed more rarely (3.7%) in rats inoc. with material which was passaged first *in vitro*, then *in vivo*, then again *in vitro*. The difference between the frequency of tumor formation in pure and mixed passaging experiments was statistically significant. The oncogenic effect could have been produced by *in vitro* passage of virus from human mammary cancer cells or by release of an oncogenic substance into the culture medium by the kidney cells. Tumors which formed in controls kept near the experimental animals, could have been the result of infection. In 37 rats inj. immediately after birth with fluid from a culture of human malignant cells (strain 558 M1), no malignant growths were found.

63-1126 COMMENTS ON VIRAL NEOPLASIA. (E.) Furth, J. (Francis Delafield Hosp., New York). *Acta Un. Int. Cancr.* 19(1-2):243-246, 1963.

The role played by tropic hormones and the host's thymus is discussed in relation to the initiation and promotion of virus-induced tumors. The number of adult mice of a mammary-tumor-free strain which developed mammary tumors after inoc. with mammotropic hormone (MTH) + Bittner Virus (BV) + DES (diethylstilbestrol?) was 8/18; MTH + BV, 8/19; BV, 0/30; DES + BV, 0/30; MTH + DES, 0/22; and MTH or DES or neither, 0/77. The number of mammary tumor takes after transplantation to W9 females and males was 4/60 and 0/38, resp.; the number of takes when females and males were treated with MTH was 95/97 and 3/3, resp. In a similar experiment using W9a mice, takes for females and males were 40/43 and 0/17, resp., and for MTH-treated females, 16/16. Hormone dependent and independent transplanted tumors were histologically indistinguishable.

63-1127 STUDIES ON SUBVIRAL TUMORIGENESIS: CARCINOMA DERIVED FROM NUCLEIC ACID-INDUCED PAPILLOMAS OF RABBIT SKIN. (E.) Ito, Y. (Dept. Microbiol., U. Washington Sch. Med., Seattle). *Acta Un. Int. Cancr.* 19(1-2):280-283, 1963.

Domestic rabbits of the New Zealand white breed were inoc. with DNA (approx. 100-500 µg/ml,

0.1 ml/site by the intradermal and puncture method) from glycerinated papillomas of cotton-tail rabbits. Of 9 test rabbits which developed papillomas, all evolved into typical squamous cell carcinomas after 9-12 mo.; there were metastases to lung in 1/9, and to lung and lymph nodes in 2/9. Rabbits were also inoc. with DNA from carcinomas of virus (V)-induced and nucleic acid (NA)-induced papillomas, their lymph nodes and lung metastases, Vx7 (Rous) carcinomas and carcinomas from V-induced papillomas treated with 20-methylcholanthrene (20-Me). No papilloma developed in 4 rabbits inoc. with DNA from lymph node metastases (from NA-induced), in 23 rabbits inoc. with DNA from lung metastases (V- or NA-induced), in 12 inoc. with DNA from V + 20-Me primary lesions or in 65 receiving DNA from Vx7-induced primary tumors. Papillomas were obtained in 8/94 rabbits receiving DNA from V- or NA-induced primary tumors. Of these, 6 regressed at 8-10 wk., 1 grew weakly at 6 mo., and 1 progressed after 11 mo. to a malignant necrotic lesion which metastasized to the regional lymph nodes. (See also CRA 1(2):#145 and *ibid.*, (6):#1128, 1963.)

63-1128 TUMOR-INDUCTION WITH NUCLEIC ACID PREPARATIONS FROM CARCINOMAS OF SHOPE PAPILLOMA-CARCINOMA COMPLEX. (E., Abstract) Ito, Y. (Dept. Hygiene, Natl. U. Nara, Japan). *Proc. Am. Assn. Cancer Res.* 4(1):31, 1963.

Phenolic extracts of the transplantable Vx7 carcinoma (Rous) containing a highly viscous nucleic acid soln. were inoc. into domestic rabbits (0.2 ml. in phosphate-buffered saline pH 7.5, inj. into the skin). After 40 days small papillomas were detectable in 8 sites in 208 inoc. This rate of "take" (3.6%) is close to that caused by nucleic acid from primary carcinoma tissue (4.0%) and indicates a possibility for existence of functioning "viral" nucleic acid in the transplantable tumor. (See also CRA 1(2):#145 and *ibid.*, (6):#1127, 1963.)

63-1129 A VIRUS FROM MAMMARY TISSUE OF RATS TREATED WITH X-RAY OR METHYLCHOLANTHRENE (MC). (E., Abstract) Payne, F. E. (Dept. Epidem., U. Michigan Sch. Publ. Health, Ann Arbor), C. J. Shellabarger, and R. W. Schmidt. *Proc. Am. Assn. Cancer Res.* 4(1):51, 1963.

In one experiment a virus was isolated from mammary tissues of Sprague-Dawley rats 14 and 30 days after X-irradiation, and 14 days after 20-methylcholanthrene treatment. However, in a subsequent experiment no agent could be isolated on sampling at 3-day-intervals for up to 33 days after X-irradiation. In 1 experiment, serologic evidence suggested that the virus became more prevalent in X-ray-treated mice, and that this was associated with a high tumor frequency. However, another series of animals developed tumors with

ual frequency after X-ray treatment, without y evidence for a viral agent. No differences uld be detected between rats with or without idence of infection in histologic tumor type, equency, and time of appearance after irradiation. The isolated virus was cytopathogenic to t embryo cell cultures, was related to Toolan's viruses and Kilham's rat virus, was inhibited 5-fluorodeoxyuridine, measured 22 mμ in ameter and contained 12 capsomeres.

1130 STUDIES OF THE PLASMA LACTIC DE-HYDROGENASE-ELEVATING VIRUS (PLDEV) IN MICE. (E., Abstract) Plagemann, P. G. W. Dept. Microbiol., Western Reserve U., Cleveland, (io) and H. E. Swim. Proc. Am. Assn. Cancer Res. 4(1):53, 1963.

e plasma lactic dehydrogenase-elevating virus (PLDEV) associated with Sarcoma 180, uschka-Klein, and Hepatomas 129 and 134 in in vivo did not multiply when these tumors were opagated serially in vitro; cells grown in vitro e serially transplantable without any evi- nce of PLDEV. The tumor growth rate was the e in normal and PLDEV-infected mice. A nergistic effect on lactic dehydrogenase levels s observed when Sarcoma 180-bearing mice were ected with PLDEV, but not for the other en- es affected by the virus. Primary cultures mouse spleen, lung, or embryo, produced PLDEV r several wk. without cytologic evidence of l damage. Infection of cell cultures with DEV did not result in an increase in the rate lactic dehydrogenase synthesis, total protein ucleic acid synthesis, or in leakage of the yme from cells. Analysis indicates that DEV is of the RNA type and contains lipid.

1131 GROWTH CURVE OF A MURINE LEUKEMIA VIRUS IN MICE. (E., Abstract) ischer, F. J. (NCI, Bethesda). Proc. Am. Assn. Cancer Res. 4(1):55, 1963.

ic. of a standard dose of the Rauscher murine kemia virus into 7-week-old BALB/c mice followed within 24 hr. by disappearance the virus from the plasma and spleen. After ays the virus increased exponentially and ched a plateau on day 7-14. The viral growth ves were identical in plasma and spleen and ibited similarities to those of nononcogenic rotizing viruses. (See also CRA 1(1):#101 and d., (6):#1132, 1963.)

1132 PATHOGENESIS OF A MURINE STEM-CELL LEUKEMIA INDUCED BY A NEWLY ISOLATED US. (E.) Rauscher, F. J. (NCI, Bethesda). J. Nat. Onco. Int. Cancr. 19(1-2):368-373, 1963.

ditional studies on the Rauscher leukemogenic us are presented. Shortly after inoc. of born or adult mice with the potent virus

isolated from tissues of BALB/c mice, an intense erythropoiesis developed; 80-100% developed palpable spleens within 12 days and succumbed between 25-50 days, with evidence of enlargement of thymus, liver lymph nodes and spleen (50-70 fold increase in wt.). Leukemic tissue was easily transplanted and was very active. In mice that survived, the erythropoiesis was followed by lymphocytic leukemia which developed within 20-45 days after inoc. A 10^{-8} log dilution of virus extracts from spleen or plasma of infected mice induced the disease in more than 50% of BALB/c mice (0.05 ml i.p. when 3-5 days old) within 4 mo. When a 10^{-7} dilution of virus extracted from plasma or leukemic tissues was inoc. into mice, 50% developed disease within 95 days. Inoc. of BALB/c mice with large doses of virus (0.01 ml/g of a 1:10 dilution i.p.) at the following ages in days: 1, 3, 10, 19, 24, 32, 46, 53, and 130, induced the disease in 100% with the av. latent period to the development of palpable spleens in 50% not differing substantially, while the av. latent period for death of 50% in days was 24; 29; 29; 31; 35; 39; 43; 45; and 56, resp. Admin. of 10^3 virus doses (log ED₅₀/ml) to groups of mice (28-30 days of age) of different strains, resulted in the following incidences of disease: in 28-30 day old BALB/c, 100%; DBA/2, 100%; Swiss, 94%; C3H (mammary tumor agent (MTA) present), 100%, C3H (MTA absent), 69%; CFW, 62%; PRI, 50%; C57Bl, 12%; and AKR, 6%. Results after a dose of 10^6 admin. to 2-day-old mice were: BALB/c, 100%; DBA/2, 33%; Swiss, 92%; C3H (MTA absent), 90%; C57Bl, 100%; AKR, 90%. The same dose in 1-day-old Osborne-Mendel rats produced disease in 98%. Erythropoiesis was absent in C57Bl mice and in the rat, although leukemia developed as in other groups. The virus was present in relatively high conc. in spleen, plasma, kidney, liver, thymus, lung, brain, muscle, and lymph nodes. The virus was ether-labile, and was inactivated on incub. at 37°C for 1 hr., or at 56°C for 30 min. It was stable in antisera against Schwartz, Friend, or Moloney viruses, on exposure to formalin (1:250 dil.), on lyophilization, and on storage at -70°C or at 4°C for over 1 mo. (See also CRA 1(1):#101 and ibid., (6):#1131, 1963.)

63-1133 TISSUE CULTURE OF THE AGENT OF RETICULUM CELL SARCOMA. (E., Abstract) Soule, H. D. (Detroit Inst. Cancer Res., Mich.) and P. G. Stansly. Proc. Am. Assn. Cancer Res. 4(1):64, 1963.

Alternation of tissue culture and animal passage of an agent inducing reticulum cell sarcoma in BALB/c mice resulted in an increased incidence (from 33% to 100%) and a decreased av. latency (from 290 to 218 days) when the 2nd and 6th tissue passages were compared. Failure to obtain transmission of the disease at a 1:1000 dilution or greater with animal extracts, and successful transmission with tissue cultures from the same extracts at a final dilution of 1:10¹³ substantiates

that replication of the agent has occurred. The neoplastic diseases induced with the tissue culture fluids were: reticulum cell sarcoma 15%, lymphoblastic lymphosarcoma 59%, and a mixture of both, 28%. The use of tissue culture material markedly increased the frequency of an accompanying paralytic disease.

63-1134 AN ELECTRON MICROSCOPE STUDY ON THE DEVELOPMENT OF SV40 VIRUS. (E.)

Granboulan, N. (Inst. Sci. Res. Canc., Villejuif, Seine, France), P. Tournier, R. Wicker and W. Bernhard. *J. Cell. Biol.* 17(2):423-440, 1963.

The development of SV40 virus in kidney cells from the African green monkey was followed by serial electron microscopic observations performed between 3 hr. and 11 days after infection. In a few cells, virus particles could be observed as early as 10-12 hr., more frequently at 24-48 hr., always in the nucleus, and in close contact with the chromatin. The particles measured 33 μ , had no membrane and were arranged in crystal-like structures. Concomitant with virus infection there was hypertrophy of the nucleolus with formation of chromatin-like material and/or granulation followed by unusual dense condensations in contact with the nucleoloneme. Other secondary changes after infection were margination, or more frequently disappearance of chromatin, and the presence of fibrillary bundles in virus-containing areas. Some cytoplasmic virus particles appeared to be larger (about 50 μ). Similar changes were observed in kidney cells from the baboon (*Papio papio*).

63-1135 INHIBITION BY 5-IODODEOXYURIDINE (IUDR) OF THE ONCOGENIC EFFECTS OF HUMAN

ADENOVIRUS TYPE 12 IN HAMSTERS. (E., Abstract) Huebner, R. J. (Publ. Health Serv., Bethesda), A. D. Welch, P. Calabresi and W. H. Prusoff. *Proc. Am. Assn. Cancer Res.* 4(1):30, 1963.

Of 15 newborn hamsters inj. with a prototype pool of adenovirus type 12 ($>10^6$ tissue culture doses s.c.) and concomitantly, 5-iododeoxyuridine (IUDR; 0.5 mg s.c. then repeated every 48 hr. x 9), all survived beyond day 60, although 1/15 developed a tumor on day 39. Similarly, of 15 hamsters inj. i.p. with virus and IUDR, 11 survived 60 days, with 6/15 developing neoplasms with a mean lag of 10 days in tumor appearance compared to untreated controls. In untreated hamsters inj. with virus (s.c. or i.p.), 90% developed tumors in 40 days, all died within 60 days. No appreciable effect on tumor induction or host survival was observed when virus was inj. s.c. and IUDR i.p., or vice versa.

63-1136 VIRUS INDUCTION AND CELL-METASTASIZATION DURING TUMOUR DEVELOPMENT IN CHICKENS HATCHED AFTER CULTIVATION OF FOWL SARCOMAS ON THE EMBRYONIC CAM. (E.) Dyadkova,

A. M. (Inst. Oncol. AMS USSR, Moscow). *Acta Un. Int. Cancr.* 19(1-2):287-289, 1963.

Single application on the chorioallantoic membrane (CAM) of either of 2 filterable fowl sarcoma viruses, strain N 5 or the Engelbreth-Holm strain caused appearance of sarcoma-like growths and small sarcomas within 5-13 days in 5/17 embryos 7/52 hatched from infected eggs died within 3 w with tumor in liver or lung. In addition many the chicks developed hemorrhagic disease leading to death within 3 days to 3 wk. Application to the CAM of either of 2 nonfilterable fowl sarcomas, the MCh-659 (from a methylcholanthrene induced tumor), and the Ivanova strain (from a spontaneous sarcoma), failed to result in multiple hematomas on the membrane or chicks. Tumor growth in chicks was slower, although 7/24 died of liver and lung tumors 14-25 days after hatching. Microscopically the tumors from filterable and nonfilterable sarcomas were similar, but the author suggests that those arising from nonfilterable tumors arose through metastasization from the CAM.

63-1137 PRODUCTION OF VERTICALLY TRANSMISSABLE LEUKEMIAS WITH THE AID OF AN EXTRACT FROM A PULMONARY ADENOCARCINOMA. (Fr.) Rudali (Radium Inst., Paris) and P. Jullien. *Acta Un. Int. Cancr.* 19(1-2):382-384, 1963.

Newborn mice (107 of strain XVII/G, 91 of strain C57Bl) were inoc. with the supernatants from the 30th passage of T.P. 10438 pulmonary adenoma (from a female XVII/G given methylcholanthrene; 0.1 ml of homogenate supernatant, method of Gross) with only 30 XVII/G and 24 C57Bl mice surviving at 250 days. Among the survivors 11/30 XVII/G and 7/24 C57Bl developed leukemias all type B reticulosarcomatoses, with a mean survival of 339 and 394 days, resp. There were no pulmonary tumors. The rate of spontaneous leukemia was 0.2% and 1.8% for the XVII/G and C57Bl strains, resp. Extracts from 4 of the leukemias appearing in XVII/G mice were inoc. in 30 1-week-old mice of the same strain, with 14 surviving 250 days and 7/14 developing leukemias, with a mean survival of 422 days. The F1 and F2 of the same XVII/G animals, when inbred had leukemias in 6/36 F1 and 2/12 F2, with mean survivals of 482 and 333 days, resp. Extracts from the T.P. 10438 tumor failed to produce leukemias in AKR mice before the age of 200 days, and extracts of the transplantable lymphosarcoma L 9928 (from an earlier, chemically induced leukemia in XVII/G mice) also failed to produce leukemias in XVII/G or AKR mice. It is concluded that the T.P. 10438 contains a leukemogenic agent for XVII/G and C57Bl mice, and that this extract also inhibits the spontaneous pulmonary tumors usually observed in XVII/G mice.

63-1138 THE ACQUISITION OF CELLULAR RESISTANCE TO POLYOMA VIRUS DURING EMBRYONIC

DIFFERENTIATION. (E.) Vainio, T. (State Serum Inst., Helsinki, Finland), L. Saxén and J. Toivonen. Virology (New York) 20(2):380-385, 1963.

essentially identical to the work reported in CRA 1(5):#937, 1963.

63-1139 TRANSFORMATIONS OF HUMAN CELLS BY VIRUSES. (E., Abstract) Potén, J. (Wistar Inst. and U. Pennsylvania, Philadelphia), A. Ravdin, and H. Koprowski. Proc. Am. Assn. Cancer Res. 4(1):53, 1963.

Cultures of adult or embryonic skin and stable diploid fibroblastic strains of human origin were transformed to epithelial-like cells after exposure to simian virus 40 (SV40). (See CRA 1(3):#480, 1963.) On implantation into hamsters and mice the transformed cells persisted longer than the normal cells, but they did not grow progressively. Homografts of transformed cells failed to grow in cancer pts., but implantation of the cells in 2 of the original donors gave rise to small nodules which ultimately regressed. Autopsy of 1 nodule showed sarcoma-like characteristics. The histologic picture and tissue culture studies suggest immunological mechanisms of rejection.

63-1140 THE ROLE OF SV40 (SIMIAN VIRUS 40) IN THE TRANSFORMATION OF HUMAN CELLS. (E.) Koprowski, H. (Wistar Inst, Philadelphia), and J. T. Proc. Roy. Soc. Med. 56(4):252, 1963.

After a review of earlier work (see CRA 1(3):#480, 1963), additional details are given of results obtained on transformation of human embryonic and adult fibroblasts by simian virus (SV) 40 in tissue culture. The transformed cultures always yielded SV40, whereas noninfected controls remained free of virus. The most consistent of many chromosomal aberrations observed in the transformed cultures were related to the secondary constrictions of the chromosomes. Cloning of infected transformed cultures resulted in isolation of two types of cells: clones of epithelial-like cells always yielding virus, and consistently virus-free clones of fibroblast-like cells.

63-1141 THE EFFECT OF ERYTHROPOIETIN ON THE ERYTHROPOIETIC RESPONSE IN THE FRIEND VIRUS DISEASE. (E., Abstract) Mirand, E. A. (Roswell Park Mem. Inst., Buffalo) and J. T. Proc. Am. Assn. Cancer Res. 4(1):44, 1963.

Endogenous erythropoietin levels were not increased in plasma or spleens of mice showing a greatly increased erythropoietic activity due to infection with Friend's virus. However, administration of exogenous erythropoietin to mice significantly enhanced the erythropoietic response by decreasing the latent period and increasing the hemato-

crit. Mice receiving erythropoietin for 3 days before and 7 or 11 days after virus infection had hematocrits of 63% and 82% on days 8 and 15, resp. These values are greater than those found in mice receiving erythropoietin or virus alone. Exogenous erythropoietin did not affect the peripheral leukocyte counts of infected animals, but caused a 2-3x increase in spleen wt., as compared to spleen wt. of mice receiving erythropoietin or virus alone.

63-1142 ON THE TENTATIVE ROLE OF INFECTIOUS VIRUSES IN TUMOUR ETIOLOGY. (E.) Mazurenko, N. P. Acta Un. Int. Cancr. 19(1-2):235-238, 1963.

The number of deaths from leukemia after administration of various strains of vaccinia virus (ovovaccinia, neurovaccinia or dermovaccinia; diluted 1:20 or 1:40, s.c. or i.p.) to 12 hr. to 15-day-old CC57Br substrain mice was 69/351 surviving 6 mo.; and after administration of influenza virus, 6/40 deaths in those surviving 6 mo. Newcastle virus in CC57Br substrain, vaccinia in CC57W and C3H, influenza virus in C3H and vaccinia in white non-inbred mice gave negative results in 327 animals surviving 6 mo. After vaccinia administration 1/139 CC57Br mice died of leukemia. Mortality was high in newborn CC57Br substrain mice, and virus could be isolated from survivors only during the following 2-3 wk. Adults were refractory. Mice of CC57Br, CC57W, C57Bl, and C3H strains were about 90% susceptible and white rats 70-90% susceptible to the hemocytoblastosis-reticulosis virus. This virus, which differs from vaccinia, was isolated regularly from CC57Br substrain mice with vaccinia induced leukemia. The author suggests that the nontumor viruses may produce conditions favorable for the manifestation of the specific tumor virus.

63-1143 COMPARISON OF ROUS SARCOMA WITH SARCOMA XC BY PRECIPITATION IN AGAR. (E.) Gusev, A. I. (Inst. Epidem. Microbiol., Acad. Med. Sci. USSR, Moscow) and J. Svoboda. Folia Biol. (Praha) 8(3):140-142, 1962.

Tumor and normal tissue extracts in physiological saline (1:5 at pH 6.8-7) were used as antigens. Antisera against Rous sarcoma and normal fowl tissues were obtained by immunizing rabbits. Eluates of antibodies against sarcoma XC and rat muscle were prepared from rabbit antisera against fowl muscle. Two ml antiserum against fowl muscle gave 0.4 ml antibody eluate against rat muscle or 0.3 ml antibody eluate against sarcoma XC. Antigens, antisera and antibody eluates were tested via microprecipitation in agar. Soluble species specific fowl antigens were not found in transplantable rat tumors (XC, R₂, XCBK) induced in rats by Rous sarcoma. These sarcomas, together with transplantable 3,4-benzpyrene-induced rat sarcomas, Rous sarcoma, duck sarcoma and rat, fowl and duck muscle all contain a common heterogenetic antigen.

63-1144 DATA CONCERNING THE VIRAL AETIOLOGY OF HUMAN CUTANEOUS RETICULOSARCOMA. (E.)

Cajal, N. (Inst. Inframicrobiol., Bucharest, Rumania), M. Cepleanu, N. I. Ionescu and S. Dumitrescu. Rumanian Med. Rev. 7(1):79-81, 1963.

Serial passage into chick embryo chorioallantoic membrane of (1) triturated tumoral tissue from 2 human cutaneous reticulosarcomas, (2) chorioallantoic membrane suspensions of the same, (3) tumor filtrates which had been passed through a Seitz K5 filter, all resulted in similar lesions. Upon electron microscopic examination the cells exhibited corpuscular formations of polygonal shape and a uniform size of about 30 μ . In addition, the presumed infectious agent still remained infective in glycerol at 4°C and in normal saline at -15°C for a period of 245 days. The agent was destroyed by heat (100°C for 20 min.). Invariably all the lesions, regardless of the manner in which the inoculum was made, exhibited the same pattern.

63-1145 INHIBITION BY 20-METHYLCHOLANTHRENE OF INTERFERON PRODUCTION IN RAT CELLS. (E.)

De Maeyer, E. (Dept. Virol, Rega Inst., U. Louvain, Belgium) and J. De Maeyer-Guignard. Virology 20(3):536-539, 1963.

Preincubation of secondary cultures of rat embryo cells (RE) or of rat tumor cells (DE7R) with 20-methylcholanthrene (20-Me) 10 μ g/ml in ethanol for 16 hr., or 1-10 μ g/ml in acetone, dried in the culture flask prior to cell seeding, failed to affect virus titers (10⁵-5-5.6) for the RE cell vaccinia virus or for the DE7R cells-Sindbis virus systems (control cell titers were 10⁵-1-5.8). However on subsequent assay for interferon production a consistent decrease was observed in all 20-Me-treated culture fluids. In both cell-virus systems interferon activity (determined by ability to prevent plaque formation on overnight preincubation of cell cultures with interferon-containing dialyzed culture fluid prior to virus seeding) was decreased by about 50% in 20-Me-treated cultures. Incubation of preformed interferon with 20-Me had no effect on interferon activity, indicating that 20-Me inhibits synthesis rather than activity. The 20-Me effect on interferon synthesis resembles that reported for some steroid hormones of related chemical structure, and suggests a new possible mechanism for activity of a chemical carcinogen on viral oncogenesis, e.g., inhibition of interferon synthesis with consequent activation of a latent oncogenic virus.

63-1146 IMMUNOLOGIC PROTECTION AGAINST CONTAMINATION OF ANTIPOLIOMYELITIS

VACCINES BY ONCOGENIC VIRUSES. (Fr.) Barski, G. (Gustave Roussy Inst., Villejuif, Seine, France). C. R. Acad. Sci. 256(17):3776-3778, 1963.

Incubation (37°C x 1 hr.) of polioviruses type I (Mahoney), type II (Linden) and type III (Saukett) grown in TG cell cultures with a rabbit antiserum to the same cultures failed to reduce the titer of the polioviruses, although the same antiserum was markedly cytotoxic to TG cultures. Incubation of a mixture of poliovirus (type I, 10⁵ ID₅₀/ml) + polyoma virus (SE strain; 10^{4.5} ID/ml) with an anti-polyoma rabbit antiserum (titer = 1:1280 against 8 HA U) with or without subsequent storage at 4°C x 11 days did not affect the infectivity of the poliovirus, but inactivated the polyoma virus completely. The antiserum-neutralized polyoma virus remained inactivated even after subsequent incubation with human gastric secretions or with trypsin (in buffer, pH 7.5).

63-1147 INTERFERENCE BETWEEN HERPES AND POLYOMA VIRUSES IN THE ADULT HAMSTER IN VIVO.

(Fr.) Barski, G. (Gustave Roussy Inst., Villejuif Seine, France). C.R. Acad. Sci. (Paris) 256(25):5459-5462, 1963.

When male and female hamsters, 3-5 mo. old, were inoc. i.p. with polyoma virus (PV; 2,000 HA U, i.p.) 31/42 survivors developed hemangiomata of the liver by mo. 3-4 with concurrent pulmonary hemangiomata in 11/31. In a comparable group, similarly inoc. with PV, but inoc. 24 hr. earlier with herpes virus (10⁴-10^{4.5} ID₅₀ i.p.), only 1/31 survivors developed a hemangioma (hepatic). Herpes virus alone, at the same dose, caused encephalitic death in 8/52; herpetic encephalitis occurred in 15/51 given PV 24 hr. later. The author suggests that the protection from polyoma afforded by pre-inoculation with herpes virus occurred as an interference phenomenon by the asymptomatic, latent systemic herpes infection, not by cross-immunity. Specific antibodies could not have played a significant role, since the most effective pretreatment interval was <48 hr. Besides, polyoma virus gave no protection against herpes virus encephalitis. It is suggested that such interference, especially immediately postnatally, could be a factor in the production or suppression of carcinogenesis.

63-1148 ALTERATION IN SPLEEN RNA FOLLOWING INFECTION WITH FRIEND LEUKEMIA VIRUS.

(E., Abstract) Rothstein, E. L. (Lab. Cancer Res., Albert Einstein Med. Ctr., Philadelphia, Pa.) and M. A. Rich. Fed. Proc. 22(2):314, 1963.

In spleens of mice infected with Friend's disease virus, the av. RNA content was 8.40 mg/g, whereas in control uninfected spleens, content was 5.48 mg/g. Base ratios of RNA extracted by the Gierer and Schramm or by the Schmidt-Thannhauser procedures were: G = 1.39, A = 1.0, C = 1.36 and U = 0.75 for infected and G = 1.19, A = 1.0, C = 0.96 and U = 0.72 for uninfected spleens, indicating an increase in the guanine and cytosine contents of infected spleen RNA. Base analysis of

the heart, liver, and kidney indicated little difference between infected and control organs, but thymus RNA of infected mice contained 20% more uracil and cytosine than uninfected spleen RNA. Preliminary experiments with the Rauscher murine leukemia virus suggest similar alterations in thymic RNA prior to development of clinical leukemia.

63-1149 TUMOR INDUCTION BY POLYOMA VIRUS IN TRANSPLANTED MOUSE TISSUES.

(Abstract) Dawe, C. J. (NIH, Bethesda), M. G. Morgan and W. D. Morgan. *Fed. Proc.* 22(2):605, 1963.

The frequency of tumors arising in isologously transplanted mouse submandibular glands infected with polyoma virus was 32/41 (78%) with adult glands; 18/30 (60%) with newborn glands; 32/64 (50%) with rudiments from 13- or 14-day embryos. Tumors appeared in 108 uninfected controls. The data reinforce previous findings in organ culture of increased tumor response to polyoma virus with advancing submandibular gland development. No tumors were induced in 66 infected transplants of lung, renal cortex, or pancreas, indicating that direct infection cannot alter the tumorigenicity shown by these organs *in situ*. Trypsin-isolated epithelial and mesenchymal components of submandibular gland rudiments infected and transplanted separately failed to induce tumors in 36 recipients, suggesting that intact epithelio-mesenchymal relationship is necessary for tumor induction by polyoma virus in mouse submandibular glands.

63-1150 AMORPHOUS TUMOURS INDUCED IN ALFALFA BY POTATO LEAFHOPPERS. (E.) Barnes, K. (Agric. Res. Ser., U. S. Dept. Agric., U. S. Forest, Pa.) and R. C. Newton. *Nature (London)* 196:95-96, 1963.

In a preliminary study it was observed that the alfalfa (*Medicago sativa*) plant 31-3 developed amorphous tumors at different sites of feeding by the potato leafhopper *Empoasca fabae*, from 3 different populations. Plants exposed to nymphs or adults, or extracts of the same, developed swellings at 30-36 hr. after initiation of treatment, followed by epidermal rupturing at 42-48 hr., and by full tumor development at 5-7 days. In plant 31-3 tumors were produced from heat inactivated (89-90°C x 11 min.) or formaldehyde (1000 ppm) treated leafhopper extracts, suggesting that the tumorigenic material was not a virus (but might possibly be a growth stimulator).

63-1151 EXTRACTION AND IN VITRO INFECTIVITY OF DESOXYRIBONUCLEIC ACID FROM POLYOMA VIRUS. (Fr.) Paoletti, C. (Gustave-Roussy Inst., Villejuif, Seine, France), G. Orth, M. Boiron, J. Lamonthézie and P. Atanasiu. *Ann. Inst. Pasteur (Paris)* 104(6):717-733, 1963.

In qualitative experiments, the method of extraction of the DNA from polyoma virus infected mouse embryo cells (phenol, papain, or sodium dodecyl sulfate), tested in mouse embryo or baby mouse kidney cells, proved not to be critical. However, in order to obtain a DNA preparation free from viral particles, it is necessary to operate with infected cells heated to 75°-100°C. The best method consists in using phenol extraction of cells heated to 80°C for 30 min. The cytopathogenic effects produced are in all respects, comparable to those induced by the virus itself but they appear later because of the low infectious titer of the extracts. The infectious DNA obtained is not pure viral DNA but rather a mixture of cellular and viral DNA in at least a 1,000:1 ratio. Mouse kidney cells appear to constitute a more sensitive system for the demonstration of DNA infectivity than mouse embryo cells.

63-1152 POLYOMA VIRUS IN EXPERIMENTAL ANIMAL COLONIES IN THE FACULTY OF MEDICINE, KYUSHU UNIVERSITY. (Jap.) Mori, R. (Dept. Bacteriol., Kyushu U., Fukuoka, Japan) and K. Amako. *Fukuoka Igaku Zasshi (Fukuoka Acta Med.)* 54(3):303-306, 1963.

Occurrence of anti-hemagglutinating antibody against SE polyoma virus in 2 colonies maintained in the Faculty of Medicine, Kyushu University was investigated using 176 mice and 2 rats during the period 1961-1963. There was no evidence of SE polyoma virus infection in the mouse colonies investigated, nor in 4 mice bearing tumors.

63-1153 PERSISTENT INFECTION OF L CELLS WITH POLYOMA VIRUS: PERIODIC DESTRUCTION AND REPOPULATION OF THE CULTURES. (E.) Henle, G. (Virus Lab., Child. Hosp. Philadelphia, Pa.), H. C. Hinze and W. Henle. *J. Nat. Cancer Inst.* 31(1):125-141, 1963.

Persistent infection with polyoma virus (strain 105) was established in monolayers of Earle's L cells and of the L(M) line, although monodispersed suspended L cells failed to support persistent infection. The infection led periodically to extensive cellular destruction with concomitant increase of infected cells (detected by immunofluorescence, mainly cytoplasmic), and by periods of repopulation accompanied by decreases in the infected cell proliferation and by a predominantly nuclear antigen localization. Cells containing virus tended to occur in foci, suggesting spread partly by contact. Addition of antipolyoma serum to carrier populations improved the culture's appearance and reduced the incidence of staining cells, but final cures could be obtained only after several mo. of continuous treatment. Attempts to demonstrate an interaction of interference and interferon in this system, yielded equivocal results, suggesting that other undetermined factors are probably involved in the maintenance of the persistent infection.

- 63-1154 DIFFERENCES IN RESPONSE OF HAMSTER TUMOR CELLS INDUCED BY POLYOMA VIRUS TO INTERFERING VIRUS AND INTERFERON. (E.) Henle, G. (Virus Lab., Child. Hosp. Philadelphia, Pa.) and W. Henle. J. Nat. Cancer Inst. 31(1):143-153, 1963.

The H-1 and H-2 cell lines derived from tumors induced in hamsters by inoc. at birth with polyoma virus (PV) were free from and resistant to PV infection. The 2 lines were similar in morphology, cultural growth patterns, capacity to produce tumors in weanling hamsters, and susceptibility to Newcastle disease virus (NDV) and to vesicular stomatitis virus (VSV), but differed slightly in acid production. In addition, H-1 cells and their various sublines showed moderate or no protection after exposure to UV-inactivated NDV (NDV_{UV}) when challenged with NDV or VSV, and they could not be rendered resistant by any interferon tested; irregularly the cells produced an interferon ineffective in homologous and H-2 cultures, but active in hamster embryo and Earle's L cell cultures. In contrast, the H-2 cells could be rendered resistant by NDV_{UV} and interferon, whether the latter was derived from homologous, hamster embryo, or L cell cultures. The H-2 cultures also produced a potent interferon active in hamster embryo or L cell cultures. Protection was more pronounced in homologous than in heterologous systems. An H-3 tumor line appeared to react like the H-2 line. Results suggest that lack of response to interfering virus and interferon are not a reliable criterion of malignancy.

- 63-1155 TRANSPLANTATION OF POLYOMA TUMOURS IN RATS. (E.) Vandeputte, M. (Rega Inst., Louvain, Belgium) and P. De Somer. Nature (London) 199:391-392, 1963,

Pretreatment of R strain adult rats with the homologous transplantable polyoma kidney sarcoma (LKS₁; 3 weekly s.c. inj.) resulted in partial resistance to subsequent tumor isografts. Challenging isologous tumors rejected were: a transplantable kidney sarcoma (RKS₇; 5 x 10⁵ cells) 5/6; a continuous tissue culture from a primary polyoma kidney sarcoma (38K; 5 x 10⁵ cells) 3/4; and an R rat embryo fibroblast line transformed *in vitro* by polyoma virus (PV) (REPT; 5 x 10⁵ cells) 3/6. All 3 tumor lines failed to yield PV. Isograft rejection did not occur on challenge of 4 immunized rats with a cell line derived from a carcinogen-induced mammary tumor in an R rat (DE7R; 1 x 10⁴ cells). Resistance was not observed in similarly challenged rats preimmunized with a homologous transplantable Lewis benzpyrene sarcoma (LBPS₁), normal trypsinized and washed Lewis kidney cells, or control medium (Eagle's basal + 10% calf serum). Adult rats immunized with the LKS₁ tumor or with partially purified PV developed partial resistance to subsequent challenge with the REPT tumor (5 x 10⁵ cells) 5/8, and also to a tissue culture

line derived from a primary s.c. fibrosarcoma induced in an R rat (33F). The degree of resistance was related to size of the inoculum. Partial resistance was also obtained in newborn rats immunized with PV (12/24 resistant to 1 x 10⁶ 33F cells). Approx. 50% of the PV-immunized newborn animals developed polyoma tumors prior to isografting. Results indicate that specific resistance to polyoma tumor isografts may be obtained by pretreatment with homologous, apparently virus-free polyoma tumors or with the PV virus, degree of resistance depending on isograft size. In virus-immunized animals, resistance may be due to induction by the virus of an antigen from the infected host cells which leads to isograft rejection and failure to develop tumors. In newborn, immunologically incompetent animals, virus-induced tumor cells can proliferate and eventually give rise to tumors. Thus the resistance to isografts (5/6 at 1 x 10⁶ but 0/1 at 5 x 10⁷ 33F cells) observed in tumor-bearing adults inoc. at birth with PV is unexplained. A possible explanation may be due to quantitative differences in the immunologic response, depending on tumor population size. Thus animals developing immunologic reactivity may be unable to reject an already relatively large PV-induced tumor cell population, but could reject the relatively small tumor population provided in the isograft.

- 63-1156 STUDIES OF THE NATURE OF POLYOMA VIRUS STRAIN BBT₂. DISSERTATION FROM THE DIVISION OF BIOLOGICAL CANCER RESEARCH OF THE INSTITUTE OF MEDICINE AND BIOLOGY OF THE GERMAN ACADEMY OF SCIENCES IN BERLIN. (Ger.) Urbach, D. Wiss. Zschr. Humboldt Univ. Berlin (Math. Naturwiss.) 12(2):309, 1963.

Polyoma virus BBT₂ isolated by tissue culture from the mouse strain Agnes Bluhm was found to be very resistant to a number of chemical and physical noxa such as temperature, oxygen, ether, desoxycholic acid, proteolytic enzymes, and nucleases. Inactivation could only be brought about with formalin. Results of a study on latency of the virus infection showed that approx. 50% of all untreated normal as well as leukemic mice proved to be infected with BBT₂ virus. Mouse embryonal cultures could be infected by the isolated virus DNA and a cell-free extract of the infected cultures retained this infectivity. The culture medium of such infected tissue cultures induced tumors in rats and mice. The DNA isolated from tumors induced by the polyoma virus BBT₂ failed to produce cytopathological changes in tissue culture cells.

- 63-1157 NEW METHOD FOR DETECTION OF MOUSE MAMMARY TUMOR VIRUS. I. INFLUENCE OF FOSTER NURSING ON INCIDENCE OF HYPERPLASTIC MAMMARY NODULES IN BALB/cCRL MICE. (E.) Nandi, S. (Dept. Zool., U. Calif., Berkeley). J. Nat. Cancer Inst. 31(1):57-73, 1963.

method is presented for the rapid detection of mouse mammary tumor virus (MTV), with hormone-induced nodulogenesis in the mammary gland of intact female or gonadectomized (at 35 days) mice of the BALB/cCrgl strain, treated from day 36 with 17 β -estradiol (1 μ g/day) + deoxycorticosterone acetate (500 μ g/day) for 90 days. Treated males and females foster nursed on MTV-free strains BALB/cCrgl, C57Bl/Crgl, A/Crgl, C3H/Crgl/2, and 1S/Bi failed to develop mammary nodules 22 days after discontinuation of hormone, with the exception of 1 nodule which appeared in 1/14 females foster nursed on C3Hf/Crgl mothers. Mice nursed on the MTV strains C3H/Crgl, A/Crgl, A/Crgl/3, DBA/2NCrgl, and R111/DmCrgl developed a mean of 1.4-11.5 (2.7-19.0 mammary nodules for males and females, resp. Mammary nodules were most frequent in males or females foster nursed by C3H/Crgl or A/Crgl mothers, and in females foster nursed by DBA/2NCrgl or A/Crgl/3 mothers. The R111/DmCrgl strain used in this experiment is known to undergo spontaneous reduction in mammary tumorigenesis (to 15% in the present experiment) and this strain gave the lowest incidence of nodulogenesis (1.4 in males; 2.7 in females) on foster nursing, suggesting that the test for MTV may have quantitative value. "Noduloids" observed in some females are described and differentiated from true nodules.

1158 NEW METHOD FOR DETECTION OF MOUSE MAMMARY TUMOR VIRUS. II. EFFECT OF ADMINISTRATION OF LACTATING MAMMARY TISSUE EXTRACTS ON INCIDENCE OF HYPERPLASTIC MAMMARY NODULES IN BALB/cCrgl MICE. (E.) Nandi, S. (Dept. Zool., U. Calif., Berkeley). *J. Nat. Cancer Inst.* 31(1):75-89, 1963.

Specificity of the test for mammary tumor virus (MTA) described in CRA 1(6):#1157, 1963. Tested using male and female mice inj. with saline instead of hormones, and by inoc. the test with lactating mammary tissue extracts (i.p. age 2 days) from females of various MTA-negative, and MTA-free strains. Males or females only with saline or with extracts from mammary glands of MTA-negative C57Bl/Crgl, A/Crgl, C3H/Crgl/2, or males inj. with extracts from the BALB/cCrgl strain failed to develop mammary nodules 22 days after discontinuation of hormone treatment, with the exception of 1/19 males inj. with extract from 1/4 C3H/Crgl/2 females. Males and females inj. with extracts from the MTA-positive C3H/Crgl or A/Crgl, or males inj. with extracts from the DBA/2NCrgl strains all developed mammary nodules, with mean numbers of 3.4-9.7 at 22 days. When determination of nodulogenesis was delayed to 36 days after the end of hormone treatment, mean number of nodules in females inj. with C3H/Crgl extracts increased from 5.4 to 12.0. The frequency of previously described "noduloids" decreased in glands examined 36 days after discontinuation of hormone treatment.

63-1159 PRODUCTION OF TUMORS IN SYRIAN HAMSTERS AFTER ORAL ADMINISTRATION OF POLYOMA VIRUS. (E.) Chu, E. W. (NCI, Bethesda) and A. S. Rabson. *Proc. Soc. Exp. Biol. Med.* 113(3):592-595, 1963.

Polyoma virus (mouse embryo culture fluid, 0.25 ml 2x/wk. for 16 mo., starting at age 6 wk.) admin. orally, to 20 hamsters, induced 4 s.c. sarcomas 14, 18, 18 and 44 wk. after start of experiment. In these 4 animals along with 7 others which were infected but had no s.c. tumors, at autopsy no primary tumors of the g.i. tract were found. No tumors were found in the remaining virus-fed group and in 10 controls.

63-1160 IMMUNOLOGICAL STUDIES OF THE SHOPE PAPILLOMA-CARCINOMA COMPLEX OF RABBITS. (E.) Evans, C. A. (Dept. Microbiol., U. Washington Sch. Med., Seattle). *Acta Un. Int. Cancr.* 19(1-2):110-112, 1963.

In rabbits inoc. with the Shope papilloma virus (SPV) by a standardized procedure, tumor regression occurred spontaneously in about 35%, with 90% of all regressions evident by 6 wk. after inoc., and rate or extent of regression was unrelated to level of SPV neutralizing antibody in the serum. Vaccination with living papilloma suspensions (intracutaneously, at the time of SPV infection) increased the regression frequency to 60-80%. A similar vaccination of rabbits 2-4 wk. prior to transplantation of the virus-free transplantable carcinoma Vx7 prevented carcinoma development in a large proportion of animals. There was no apparent relationship between vaccine potency against papilloma and against the Vx7 tumor growth. (See also CRA 1(2):#252, 1963.)

63-1161 IMMUNOLOGICAL STUDIES WITH POLYOMA-INDUCED TUMORS IN HAMSTERS. (E.) Defendi, V. (Wistar Inst. Anat. and Biol., Philadelphia, Pa.). *Acta Virol. (Praha) [Eng.]* 7(3):254-259, 1963.

The role of possible new antigens was investigated in a study of the immunologic response of hamsters to tumor induction by polyoma virus (PV). Efficient protection against PV tumor induction could not be obtained by ligation of virus-free PV-induced tumors, or by immunization with isologous tumors. Immunization by irradiated H61/104 tumor cells (12th transplant, 2 mo. *in vitro*), but not by the P-84 cell line (transformed *in vitro*) was obtained in 4/5 hamsters challenged with 2 x 10⁴ H61/104 transplantable tumor cells; on challenge 1 mo. later with 5 x 10⁴ tumor cells immunity persisted in only 1/4, and no cytotoxic activity was detected in the sera of any of the apparently resistant animals. Immunization of C3H/Bi mice with PV-induced hamster tumors gave a similarly short lived partial protection to subsequent challenge with C3H/Bi PV-induced tumor cells. Immunization of hamsters with PV had some

protecting effect against challenge with PV tumors induced both *in vivo* (A and H61/104) and *in vitro* (P-113), but not to the *in vitro*, PV-producing line P-130; the effect showed a high degree of dependence on challenge inoculum size. The lowered level of protection to PV tumors observed in immunized hamsters is thought due to weakening or disappearance (on transplantation or *in vitro* passage) of possible new antigen produced in primary PV-induced tumors. The hypothesis is supported by studies of tumor development in organs from PV-infected newborn hamsters transplanted into adult hamsters, where 0/28 PV-immunized hosts allowed tumor development, compared to 17/71 in non-immunized controls.

63-1162 IMMUNOLOGICAL STUDIES WITH POLYOMA-INDUCED TUMORS IN HAMSTERS. (E.) Defendi, V. (Wistar Inst., Philadelphia, Pa.). *Acta Un. Int. Cancr.* 19(1-2):115-119, 1963.

See CRA 1(6):#1161, 1963.

63-1163 INHIBITORY ACTION OF COLLOIDAL CHROMIUM RADIOPHOSPHATE ON FRIEND LEUKEMIA. (Fr.) Duplan, J.-F. (Radium Inst., Paris), C. Lévy, F. Zajdela and A. Chevallier. *C.R. Acad. Sci. (Paris)* 256(20):4320-4324, 1963.

Nonhomozygous Swiss mice (aged 30 days) treated with colloidal CrP₃₂O₄ (15 µC of P₃₂ in 0.2 ml mouse serum i.v.) at the time of Friend leukemia virus (FLV) inoc. (0.2 ml cell-free extract i.p.), showed a lowered frequency of leukemia deaths at 150 days (22% of 24). Controls receiving FLV alone or with nonradioactive CrPO₄ had leukemia death frequencies of 88% of 25 and 81% of 16, resp. Administration of the radioactive phosphate 5 days after FLV inoc. did not prevent leukemia deaths (5/8 animals, with 8/14 dead from murine hepatitis at 40 days). Autoradiographic studies showed a 48 hr. distribution of the isotope identical for FLV-inoc. (5, 10 or 17 days previously), and uninoculated mice, with predominant localization to liver and spleen macrophages.

63-1164 CYTOTOXIC ASSAYS AND OTHER IMMUNOLOGIC STUDIES OF LEUKEMIAS INDUCED BY FRIEND VIRUS. (E.) Wahren, B. (Inst. Med. Cell

Res. Genet., Karolinska Inst., Stockholm, Sweden) *J. Nat. Cancer Inst.* 31(2):411-423, 1963.

Sensitivity to Friend (F) virus (V) infection varied between complete susceptibility in DBA/2 and (C3H x DBA/2)F₁ hybrid mice to relative resistance in other DBA/2 F₁ hybrids. Sera from DBA/2 hybrid mice, resistant to F leukemic spleen homogenate or spleen cells were cytotoxic against FV-induced leukemic cells. Cytotoxic antibodies were found in the presence of H-2 antigens. Sensitivity of spleen cells to cytotoxic action increased 15-20 days after infection. Cytotoxic activity of serum antibodies appeared specific for FV-induced leukemias, as no effect was detected on 2 other V-induced tumors leukemias of varying origin, or normal spleen or lymph node cells. Sera cytotoxicity active on Gross lymphoma cells had no effect on F leukemic cells. The cytotoxic titer was markedly reduced when sera were absorbed with F leukemic cells *in vivo* and *in vitro*. Both absorptions and cytotoxic tests were performed on several independent induced F leukemias, which thus seemed to cross-react. Admixture of cytotoxic serum with leukemic spleen homogenate either inhibited tumor growth or significantly increased the time until macroscopically detectable F leukemia developed.

63-1165 POSSIBLE TUMOR SPECIFIC ANTIGENICITY IN LEUKEMIA INDUCED BY GROSS VIRUS. (E.) Slettenmark, B. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm). *Acta Un. Int. Cancr.* 19(1-2):120-123, 1963.

Adult C3H mice after pretreatment with small doses of Gross virus-induced lymphoma cells could be rendered resistant against the isologous Gross virus tumor after repeated cell inoc. of different homologous or isologous Gross tumors. Sera from resistant mice when tested for cytotoxic effect *in vitro*, in the presence of complement, against Gross tumors, showed activity between separately induced Gross lymphomas. Normal lymph node cells or C3H lymphomas of nonviral origin were not sensitive to the action of these sera. In absorption experiments lymphoma cells from Gross tumors removed the cytotoxic activity while normal lymphocytes or nonviral-induced leukemias had no effect. The results indicate the existence of a cellular antigenicity specific for all or several Gross virus-induced lymphomas.

See also abstract nos.: 1030, 1031, 1038, 1083, 1100

3-1166 BRONCHOPULMONARY CANCER (A SERIES OF 600 OBSERVATIONS). (Sp.) Purriel, P. and D. Tamalino. *Torax* 11(4):199-245, 1962.

In a general review of bronchopulmonary cancer (BPC) incidence and mortality, data are given for Uruguay (population 2,800,000) collected during a chest X-ray survey of the population in connection with a tuberculosis campaign. In 1959, out of 4396 deaths ascribable to cancer and 20,593 for all causes, 529 deaths were ascribable to BPC. These results showed an increase in BPC deaths from 8.4% of all cancers in 1943 to 12% in 1959. In addition, death by cancer for the same period increased from 11.7% to 28.6% of all deaths. Over the period 1954-1957, 1,187,357 (about 40% of the total population) chest X-rays were performed with findings of probable intrathoracic tumors in 171 cases giving an incidence (per 100,000) of 15.4. The age distribution showed 3.5 from 0-39 and 50 in those over 40. The incidence for Montevideo was 3.3 but 4.1 in the rural areas. In an analysis of the 600 observations in the authors' series, 58 were in men and 32 in women. In 96.8% of the cases there was a history of smoking (65.9% heavy smokers). The predominant histological type was squamous cell (64.5% in men, 62.5% in women) followed by adeno- and undifferentiated carcinoma, which had about the same incidence in both men and women (about 12%-15%).

3-1167 REGIONAL CHARACTERISTICS AND EXPANSION OF MALIGNANT NEOPLASMS IN KAZAKHS SSR. (Rus.) Syzganov, A. N. (Inst. Clin. Exptl. Surg., Acad. Sci. Kaz. SSR.) and N. F. Kramchaninov. *Inst. Klin. i Eksp. Khir., Akad. Nauk Kaz. SSR.* 8:3-11, 1962.

Data on cancer morbidity in Kazakhstan, given by yr. for the period 1951-1959, showed a decrease in incidence per 100,000 population from 63.3 in 1951 to 49 in 1954, followed by a steady increase to 77.5 in 1959. Marked increases were noted during this period in cancers of the esophagus (7.1 in 1951 to 13.6 in 1959), stomach (2.1 to 15.6), bronchus, lung and pleura (1.4 to 11.1); lesser increases in cancers of the rectum and skin, and decreases in cancers of the uterus and mammary glands. Rural populations showed a lower total incidence of cancers than city populations (71.8 and 85.0, resp.), but cancer of the esophagus was more prevalent in rural than in city populations (14.8 and 9.6, resp.). While the total incidence was about the same in men and women (78.1 and 77.2, resp.), some cancers were more prevalent in men than in women: lip (15.3 and 0.1); esophagus (21.1 and 12.7); stomach (8.5 and 1.9); larynx (6.7 and 5.6, resp.), whereas cancers of the mammary glands were more prevalent in women than in men (6.5 and 0.2) as were skin cancers (13.7 and 10.1). The highest total incidence as well as the highest incidence of

cancers of the mouth, lips, stomach, rectum, lungs, etc., and mammary glands were in the 60-69 yr. age group, but the highest incidence for cancers of the esophagus was at 50-59 yr., for cancers of the uterus at 40-49 yr., and for cancers of the skin and larynx at 70+ yr. A regional study showed that cancer of the stomach was much more prevalent in North Kazakhstan (28.4), Semipalatinsk (28.6) and the city of Alma-Ata (31.3) and least prevalent in Gur'yev (7.2), Dzhambul (6.7) and Tselinograd (6.7). The incidence of cancer of the uterus was highest in the city of Alma-Ata (17.5), East Kazakhstan (16.9) and Karaganda (16.2) and lowest in Gur'yev (2.7) and Kzyl-Orda (3.6); of the skin, highest in East Kazakhstan (25.6) and the city of Alma-Ata (18.8) and lowest in Tselinograd (3.7), Aktiubinsk (4.7) and Kzyl-Orda (5.7); of the esophagus, highest in Gur'yev (49.7), Semipalatinsk (36.9) and Aktiubinsk (29.0) and lowest in Dzhambul (4.6) and Kokchetav (4.8); of the lungs, bronchus and pleura, highest in Semipalatinsk (10.3) and the city of Alma-Ata (10.0) and lowest in Dzhambul (1.2) and Kzyl-Orda (2.1). Mortality from cancer increased from 2.5% in 1940 to 16.3% in 1958; this may be due not only to an increase in morbidity but also to a lack of special prophylactic help. Cancer mortality increased from 79.18/100,000 in 1957 to 86.96 in 1959. Carcinogenic factors were discussed, with a review of published data.

63-1168 CARCINOMA OF THE RECTUM AND COLON OCCURRING SECONDARILY TO INTESTINAL POLYPOSIS IN THREE SIBLINGS OF A FAMILY. (Jap.) Kurihara, Y. (Dept. Surg. Hiroshima Shikaihoken Munic. Hosp., Japan). *Nippon Ishikai Zasshi (J. Jap. Med. Assn.)* 49(10):1041-1048, 1963.

Adenocarcinoma of the rectum or colon was associated with multiple intestinal polyposis in 3 siblings: 2 males, age 36 and 48, and 1 female age 42. The father died with possible carcinoma of the rectum at age 49, the mother with carcinoma of the uterus at age 54, and the maternal grandfather died of carcinoma of the stomach.

63-1169 STRUCTURAL CHANGE OF THE STRUMA MALIGNA WITH RESPECT TO IODINE PROPHYLAXIS OF GOITER. (Ger.) Walthard, B. (Pathol. Inst., U. Bern, Switzerland). *Schweiz. Med. Wschr.* 93(23): 809-814, 1963.

A study of 60 malignant goiters removed surgically during the years 1961-62 indicates that during 25 yr. since the introduction of iodine for the prophylactic treatment of goiter, while the total incidence has remained unchanged, the incidence of forms of limited malignancy has risen sharply at the expense of the highly malignant forms. For the yr. 1954 and 1962, some of these increases were, resp.: papilloma, 8.3% and 21.7%; Hürthle

cell adenoma, 8.8% and 45%. Furthermore, these goiters of limited malignancy are now more prevalent among younger people, particularly in female pts. Among the more malignant goiters, frequencies during the yr. 1954 and 1962, resp., were: carcinoma, 16.6% and 5.0%; sarcoma, 14.0% and 8.3%; hemangioendothelioma, 14.0% and 5.0%; carcinosarcoma, 1.4% and 3.3%.

63-1170 CANCER DISEASES RESULTING FROM TRAUMA. (Ger.) Bauer, K. H. Hefte Unfallheilk. 75:51-64, 1963.

In a discussion of the problem of cancer as a consequence of occupational hazards, the impact of the increased production of carcinogenic substances since the end of the 19th century on cancer incidence is stressed. For the first time in 1951, the mortality (per 100,000 of population) due to cancer became higher in men than in women (175 and 172, resp.); and 217 and 200, resp., in 1956. In young females, the incidence of cancer is higher than in men (mostly genital carcinomas), but with increasing age, the situation is reversed. This is due to the fact that the incidence of cancer in women has remained relatively constant over the yr., and that they contribute only 10% of all the bronchial tumors. Furthermore, over 50% of genital carcinomas are cured permanently. On the other hand, cancers of all other organs except breast, genitalia and biliary tract are much more frequent in men than in women, particularly bronchial carcinoma, which increase is attributed to the increase of tar products in the external environment. After exposure to tar, the resulting tumor is always at the site of maximal exposure. Among other carcinogenic substances considered are arsenic, benzene and homologs, aromatic nitro- and amino- derivatives, chromium, X-rays, radioactive materials and asbestos. As an example of a cancer developing at the site of a recognized damage by a chemical agent, the author describes a case of bronchial cancer as a result of chronic cadmium poisoning in a 57-year-old man, after 23 yr. of contact with the chemical. While criteria for a causative relationship were fulfilled, the claims in this case were denied. Claims were also denied a circus "fire eater" who developed a bronchial carcinoma after 27 yr. of his occupation. The fact that a causative relationship between trauma and cancer is rare does not mean that it does not exist.

63-1171 ON A CAUSATIVE RELATIONSHIP BETWEEN TRAUMA AND OSTEOSARCOMA. (Ger.) Jantschew, W. G. (Med. Clin., Inst. Postgraduate Med. Education, Sofia, Bulgaria), P. Kolew, E. Jordanow, T. Natschew and D. Ptaschnikowa. Zschr. Ges. Inn. Med. 18(7):308-316, 1963.

In a study of 55 cases of osteosarcoma, a traumatic event was associated with the disease

in 22 instances. In 17 cases, the osteosarcoma was diagnosed within 2-12 mo., between 13-24 mo. in 2 cases and between 25-36 mo. in 3 cases. This relationship was observed in the 4th, 5th and 2nd decades in 8, 6, and 5 pts., resp. Most subjects were engaged in physical work or practiced sports. The conditions which must be fulfilled in order to obtain legal recognition of a causative relationship between the sustained trauma and the resulting osteosarcoma are discussed in the light of five actual cases. (1) The pt. must be completely healthy before suffering the trauma. (2) The tumor must appear at the site of trauma. (3) The trauma must be of such severity as to produce tissue damage and to induce a proliferative process. (4) The type and the histological structure of the tumor must be such that it can be assumed that it arose during regeneration of the traumatized tissue. (5) The osteosarcoma must develop within a period of time such that a direct relationship to the trauma is possible; this period of time varies according to various authors between 2 mo. and 4 yr.: this period in the cases discussed varied between two mo. and 3 yr.

63-1172 PECULIARITIES OF ACUTE LEUKEMIAS IN ADULTS AND IN THE AGED. (Fr.) André, R. and A. Combrisson. Rev. Prat. 13(16):2009-2014, 1963.

The author reviews data on acute leukemias occurring at various ages and points out the differences between leukemias in children and in adults. Statistical studies from the United States and from New Zealand show two very definite peaks in the frequency (per 100,000) of all leukemias: the first is in the 0-5 yr. age group (approx. 5), the second at over 75 yr. (approx. 24). However, whereas leukemias under 25 yr. are mostly acute, in the older age groups there is an increase in chronic forms resulting in only about 30% acute leukemias at 75+ yr. Under age 20, lymphatic leukemias are the most frequent, but they form only 20-30% of leukemias over 40 yr. Two other forms, myeloid and histiomonoblastic, predominate in the older age groups. Promyelocytic leukemia is rare below age group 30, and absent in the older pts.

63-1173 PRIMARY CANCER OF THE GALLBLADDER. (STUDY OF 40 CASES.) (Fr.) Diaz, S. I. (National U. Salvador Sch. Med., San Salvador). J. Chir. (Paris) 85(4):447-464, 1963.

In an analysis of 1959 autopsies performed at the Hospital Rosales, San Salvador, between 1951 and 1960, the incidence of cancer of the gallbladder was 0.56%, or 7.05% of all cancers. Review of 35,420 biopsies also showed 29 carcinomas of the gallbladder, or 3.1% of all gallbladder specimens. In the autopsy material, cancer of the gallbladder was 4th highest in frequency among neoplasms of the g.i. tract (11.21%), with gastric cancer

45.9%, and cancers of the pancreas and liver each 4.26%. However, the gallbladder cancer had a much higher frequency in females (10/11 pt. in the autopsy series, 27/29 in the surgical series) and was second highest in frequency among g.i. cancers of females (28.57%), after gastric cancer (37.15%). Age distribution, determined in both series was highest in the 50-59 age group (15/40). The ratio of gallbladder cancers/gallbladders examined in the surgical series was highest (6.45-8.18%) in the 50-79 age groups, with an overall frequency of 8.47%. In the present study gallstones were associated with cancer of the gallbladder in 83.33% of the cases; most of the gallbladders also showed associated inflammation. All 40 cases were adenocarcinomas, 4 of which were mucoid in type; 57.5% were classified as grade II (Broders). Other factors analyzed are symptoms, differential diagnosis, type and extent of metastases, prognosis, and treatment. The author suggests that prevention may be achieved by removal of the gallbladder in pts. over 50 yr. who show evidence of gallstones.

3-1174 BRONCHIAL CARCINOMAS AND CANCERS WITH OTORHINOLARYNGEAL LOCALIZATION OCCURRING IN HOSPITALIZED PATIENTS WITH PULMONARY TUBERCULOSIS. (Fr.) Chemin, T. (Med.-Surg. Sanatorium, Roquefraiche, Lauris (Vaucluse), France) and A.-D. Roche. Presse Med. 71(20): 1047-1049, 1963.

In a population of 200 pts. with pulmonary tuberculosis, 19 developed or had cancer, including 7 cases of carcinoma of the upper respiratory and digestive apparatus (all above age 50) and 7 cases of pulmonary neoplasms. Except in one case, the antibacterial treatment had brought about a bacteriological and radiological remission of the infection. Diagnosis of the malignancy took place from 7-20 mo. after onset of TB. While these pts. were generally in poor physical condition, the age of the pts. with pulmonary cancers varied between 45-61 yr., and all were in a generally satisfactory general condition. In all 7 cases, tumors were spinocellular epidermoid epitheliomas. In 5 cases, the TB and neoplasm appeared to develop simultaneously; in one case, the latter occurred 22 yr. after a pneumothorax. Distribution of the 5 remaining cancers was: one esophagus, one stomach, one bladder, one lymphoid leukemia, and one larynx (in this pt. TB followed local irradiation). Comparison with a group of 12 pts. with bronchial carcinomas not associated with TB, revealed that the malignancy started at similar ages.

3-1175 FOOD ADDITIVES AND CONTAMINANTS AND CANCER. (E.) Boyland, E. (Royal Cancer Hosp., London). Practitioner 190:726-730, 1963.

There is general agreement that substances which

are likely to be present in food for human consumption should be tested for toxic hazards, including cancer, yet there is not complete agreement on details of such tests. Foreign substances which may be present in food are so various that they cannot be considered as one group. If there is any risk of cancer or other diseases from the use of any particular insecticide or food additive, it is difficult to assess the advantages and disadvantages of the compound. The problem of food additives is further complicated by the discovery of natural carcinogens in food, e.g., mold contaminated ground nuts (peanuts).

63-1176 STUMP SARCOMA. (Ger.) Arens, W. Hefte Unfallheilk. 75:65-68, 1963.

A survey of the literature revealed a surprisingly low incidence of malignant tumors (carcinomas and sarcomas) developing in amputation stumps. The author describes a fatal case of highly malignant mixed fibrosarcoma and spindle cell sarcoma in a man (age 35) which developed 6-8 mo. following amputation of the leg below the knee after compound fracture. In view of the huge number of amputees, and of the numerous accidental traumas to the stump which occur later on, the author expresses the opinion that a causative relationship between any trauma and malignancy may not be as frequent as is often claimed.

63-1177 EPIDEMIOLOGY OF CANCER IN AFRICA. CANCER IN KAMPALA. (E.) Knowelden, J. (Dept. Prev. Med. Publ. Health, U. Sheffield, England). Proc. Roy. Soc. Med. 56(7):529-531, 1963.

The relative incidence of cancer (per 100,000) in the population of Kampala in Uganda decreased proportionately in relation to a relative increase in the U.S. and Norway. In males at the age of 0-4 the incidence of cancer in the Kyadondo area was 9, in Johannesburg 10, in Norway 16 and in U.S. whites 23, and U.S. non-whites 21. At age 75+ the rates were, resp., 167, 614, 1720, 2815 and 1546. For females age 0-4, the rates were 5, 7, 16, 21 and 12, resp.; for the age group 75+ they were 41, 495, 1162, 1924 and 970. There was some variation in types of cancer reported: cancer of the stomach, colon, rectum and breast was relatively less frequent in the African population, while at the same time there appeared to be a relative excess of primary liver cancer. In males in Kyadondo, Norway, U.S. white and nonwhites, resp., the incidence of stomach cancer was 1.9, 20.1, 19.2 and 15.4; colon and rectum 0.8, 8.5, 13.6 and 22.9; biliary passages and liver (primary) 6.2, 0.8, 3.1 and 2.2. Some corresponding figures for females were: stomach cancer 0.8, 11.8, 11.1 and 8.3; colon and rectum 2.4, 7.2, 15.9 and 21.8; biliary passages and liver (primary) 2.2, 1.0,

1.7 and 1.9; breast 6.8, 24.2, 33.8 and 43.6; cervix uteri 6.8, 24.2, 33.8 and 43.6.

- 63-1178 SOME ASPECTS OF THE CANCER SITUATION IN UGANDA. (E.) Davies, J. N. P. (Postgrad. Sch. Med., U. London). Proc. Roy. Soc. Med. 56(7):532-535, 1963.

The ratio of cancer pts. to total pts. in Mengo Hospital has been 0.57-0.95% over the last 6 decades. During the period 1897-1906, there were the following incidences (percentage) of tumors: hepatomas, 5%; cancer of the penis, 8%; uterus, 11%; lymph nodes, 11%; mouth/tongue, 3%; salivary glands, 8%; bone, 5%; skin, 3%; and breast was 8%. From 1952-1960 the incidences (percentage) for these same sites were: 7.8%, 7.6%, 12%, 9.7%, 1.1%, 2.6%, 1.7%, 10.6% and 4.7%, resp. The pattern type of distribution was 1/71 transitional cell papilloma, 30/71 transitional papillary carcinomas (15/30 showed squamous metaplasia), and 26/71 squamous carcinomas. The number of cases of colonic carcinoma of the cecum was high (33.3%) compared to the USA (14.3%), those of the sigmoid and pelvic regions low (18.8%; USA, 48.1%). Rates of incidence did not rise with age and this discrepancy was not associated with refusal to obtain medical care. The high frequency of squamous carcinoma of the leg, carcinoma and melanoma of the ocular conjunctivae, melanoma of the soles of the feet, primary carcinoma of the liver and penis were believed to be partly the result of environmental factors. In addition, dietary intake of serotonin in bananas and tribal customs such as circumcision, were implicated. The low alkalinity of the water may explain the low frequency of gastric cancer. In the discussion, A. White states that in Southern Rhodesia, there was a deficiency in rural Kyadondo and urban Johannesburg of breast and g.i. cancer. Esophageal cancer, the commonest single g.i. cancer, occurred commonly in the 3-4th decade; 75% in the middle third, and 25% in the lower 3rd of the esophagus. Cancer of the upper 3rd of the esophagus and hypopharynx was rare. The female to male ratio for colonic cancer was 4:1; females were also prone to rectal cancer. Lung cancer was common among mine workers and was associated with apparently premalignant skin changes resembling those of chronic arsenic poisoning. Squamous cell carcinoma below the knee was not associated with long term tropical ulceration. Thyroid carcinoma was geographically restricted to an area where the basic vegetation was acacia rather than brachystegia.

- 63-1179 WORLD HEALTH ORGANIZATION. (E.) Epidem. Vital Statist. Rep. 16(4): 279-350, 1963.

The number of pts. (per 100,000 population), hospitalized for neoplasms, and tabulated according to site, is given for 12 African countries.

- 63-1180 AN INQUIRY INTO THE LIVING HABITS OF THE PATIENT WITH BLADDER TUMOR. (E.) Tedeschi, L. G. (Boston U. Med. Ctr., Mass.), D. R. Jackson and D. E. Barber. Boston Med. Quart 14(2):52-56, 1963.

An inquiry into the living habits of 206 pts. with histologically proven bladder malignancies disclosed potential hazards inherent to employment in 36 (17.9%); of these only 1 had been involved in the manufacture of 2-naphthylamine. A family history of bladder tumors was elicited in 20 cases, 6 in brothers and 4 in fathers. Tumors in other parts of the body had been present in 37 (17.9%), and a history of urinary infections was reported by 16.4%. Information concerning non-industrial, common environmental agents (including drinking and dietary habits), and intake of arsenicals and other therapeutic agents failed to reveal any strong trend. Among the pts. were 140 (68%) present smokers and 14.5% past smokers, suggesting either the presence of a potential urinary bladder carcinogen in products of cigarette smoke, or stimulation from smoking of metabolic processes leading to synthesis of endogenous urinary bladder carcinogens. In this series the sex ratio was 160 males to 46 females, with 55% of the tumors in decade 6, 22% in decade 5, and 8% in decade 4.

- 63-1181 THOUGHTS ON DECREASED INCIDENCE OF CARCINOMA OF THE STOMACH. (E.) Lawton, R. L. (Dept. Surg., Iowa State U. Coll. Med., Iowa City). Surg. Gynec. Obstet. 116(6): 750-751, 1963.

In an editorial article, it is suggested that the reported decrease in gastric carcinoma rate may reflect improved precision in localization and diagnosis of primary lesions. In addition, increase in the number of pts. undergoing surgical resection for gastric ulcers could result in a decrease in the gastric surface in the population and thereby could conceivably contribute to a reduction in the incidence of gastric carcinoma.

- 63-1182 TRENDS IN THREE CANCER SITES. (E.) Van Duser, A. L. (Wisconsin State Board Health, Madison). Wisconsin Med. J. 62(5): 221-222, 1963.

In an analysis of data obtained by the Wisconsin State Board of Health, Division of Cancer Control, covering the yr. 1950-1961, inclusive, (1) crude cancer deaths (per 100,000), (2) av. age at death, and (3) percentage of cases reported as localized, for the periods 1950-1951 and 1960-1961, are, resp.: uterus (excluding cervix), 3.60 and 3.00, 64.10 and 68.84 yr., 54.37% and 75.76%; cervix, 4.91 and 3.68, 56.49 and 59.27 yr. 46.53% and 74.07%; breast, 14.68 and 14.29, 61.55 and 62.85 yr., 37.85% and 40.77%; lung (including trachea, bronchus, and lung), 10.56 and 15.61,

.75 and 64.75 yr., 15.14% and 17.22%. The decrease in mortality rate and increase in average age at death from uterine and cervical cancers, are clearly correlated to the larger number of localized lesions detected. Wisconsin reports approx. 160,000 yearly cytological examinations. Breast cancer detection appears unimproved, while lung cancer deaths are showing a substantial increase.

- 1183 EPIDERMOID CARCINOMA ARISING IN CHRONIC OSTEOMYELITIC FOCI. (E.)
 Adlin, E. D. (Henry Ford Hosp., Detroit, Mich.)
 and J. L. Fleming. *J. Bone Joint Surg. (Amer.)*
 45A(4):827-838, 1963.

A review of 1744 cases of chronic osteomyelitis from 4 hospitals revealed 10 complicated by epidermoid carcinoma. In an analysis of these cases plus 3 more from other sources, sex distribution was 11 males and 2 females, age range was from 37-69 yr. Duration of the osteomyelitis was 10-62 yr. with a hematogenous mode of onset in 5/13, traumatic in 4/13, paronychia in 1/13, and undetermined in the remainder. Location was in the tibia in 8/13, calcaneus in 3/13 and to thumb, elbow, and femur in 1 each. Duration of recent symptoms leading to diagnosis of carcinoma was 2-48+ mo., with 1 case discovered at autopsy. A review of 90 cases from the literature (1940-1961) is appended to the discussion (67 references).

- 1184 STUDY OF STATISTICS IN PULMONARY CANCER. QUANTITATIVE EVALUATION OF ETIOLOGICAL FACTORS IN RELATION TO PULMONARY CANCER. (Jap.) Hirayama, Y. (Dept. Immunol., Nat. Publ. Health, Tokyo) and Y. Yusa. *Gan No Rinsho (Jap. J. Cancer Clin.)* 9(3-4): 1-163, 1963.

Possible etiological agents in pulmonary cancer were studied by examination of statistics for the yr. 1950-1961 in Japan. Analyses were made according to (1) cigarette smoking, (2) air pollution, (3) occupation, (4) place of residence, and (5) miscellaneous. Incidence of pulmonary cancer in cigarette smokers was 10x that in nonsmokers. Among males, the rate is 28% higher in densely populated than in sparsely populated areas. Males working in the metal and chemical industries have a higher rate than those in agriculture and forestry.

- 1185 THE OCCUPATIONAL-SOCIAL CLASS RISKS OF CANCER IN JAPAN. (Jap.)
 Hirayama, T. (Dept. Epidemiol., Natl. Publ. Health Serv., Japan) and Y. Yusa. *Gan No Rinsho (Jap. J. Cancer Clin.)* 9(2):66-74, 1963.

Incidences of neoplasms among 4187 employed males in Japan during 1958 were analyzed according to their occupation and results were expressed as

the ratio of the numbers found in corresponding groups in 1955 (1958/1955). The 5 occupational groups were: (I) professional; (II) managerial; (III) clerical and sales; (IV) technical, production and transport; and (V) agriculture, forestry, fishery and mining. Among the "lower" classes malignancies which increased over the expected were gastric, esophageal, hepatic, dermal, pharyngeal, prostatic cancers and leukemia; those which increased among the "higher" classifications were oral, colon, rectal, pancreatic, lung, renal, bladder, testicular, brain, osseous, connective and lymphatic systems. The ratios in class V for various sites in Japan, USA and Denmark were, resp.: 1.08, 1.24, 1.08 for gastric cancers; for esophageal cancers, 0.92, 1.37, 1.22 (but 1.32, 1.05 and 0.67 in class III); for hepatic cancers, 1.04, 1.00 and no data; for laryngeal cancers, 0.91, 1.38 and no data; for prostatic cancers, 1.46, 1.12, 1.14; for skin cancers, 1.24, 1.17 and no data; for leukemia 0.95, 0.96 and no data (but 1.57, 1.01 and no data in class IV). The indexes in class I for various sites in Japan and USA were, resp.: 1.46 and 0.69 for oral and pharyngeal cancers; 1.30 and 1.01 (and 1.01 in Denmark) for cancers of the colon; 1.08 and 0.92 (0.85 in Denmark) for cancers of the rectum; 2.04 and 1.02 for pancreatic cancers; 0.98 and 0.67 (but 1.34 and 0.78 in class II) for lung cancers; 1.88 and 0.93 for renal cancers; 3.02 and 1.13 for bladder cancers; 3.32 and 1.14 for brain cancers; 1.14 and 0.60 for cancers of the bone and connective tissues; 1.21 and 0.91 for lymphomas and 1.92 and no data for testicular cancers. It was pointed out by the authors that marked increase in the incidence of gastric cancer was found in persons in agricultural, mining and metallurgical fields, and marked increase in the incidence of leukemia was found in persons in overland transportation, manufacturing or rubber and rubber products and in police and security workers.

- 63-1186 PRIMARY ADENOCARCINOMA OF THE CERVIX UTERI. (E.) Marcus, S. L. (Dept. Obstet. Gynec., Cornell U. Med. Coll., New York) and C. C. Marcus. *Am. J. Obstet. Gynec.* 86(3): 384-396, 1963.

A study group of 56 cases of primary adenocarcinoma treated during the period 1933-1961 comprised 2.3% of all gynecological malignancies and 4.8% of all cervical carcinomas. The av. age of the pts. was 52.2 yr.; 12 were 50-59, 18 were over 60, 5 were under 35. The proportion of Jewish women (8/50 where religion was known) was relatively higher than would be expected in pts. with squamous cell carcinoma of the cervix. Only 2 pts. were unmarried, 14 were nulliparous, 16 had born 1 child and 7 were grand multiparas. No adenocarcinoma *in situ* lesions were encountered in this series although such changes were occasionally observed adjacent to obviously invasive lesions.

63-1187 RESULTS FROM THE TREATMENT OF GASTRIC OR CARDIAL CARCINOMA AT THE CENTRAL ARMY HOSPITAL IN 1950-1960. (Cz.) Lišková, M. (Inst. Intern. Dis., Prague, Czech.). Rozhl. Chir. 42(6):361-368, 1963.

Among 159 pts. with gastric or cardiac carcinoma treated during a 10-year-period, 69.1% were age 50-70, (range 24-86); 67.9% were male, 32.1% were female pts.; 14.4% were in professional work; 12.5% were laborers; and 8.7% were housewives. There was a family history of cancer in 37% (14% of gastric cancer); 9% had a family history of gastric or duodenal ulcers; 20% were Rh-. Incidences in blood groups were: 0, 29.7%; A, 42.6%; AB, 9%.

63-1188 CAN THE DEVELOPMENT OF A GASTRIC CARCINOMA, FOLLOWING GASTRIC SURGERY, BE CONSIDERED A MANIFESTATION OF A POSTRESECTION SYNDROME? (A DISCUSSION OF ETIOPATHOGENESIS IN CARCINOMA OF THE STOMACH AFTER PARTIAL GASTRECTOMY.) (Ger.) Rapant, V. (Surg. Clin., Palacky U., Olomouc, Czech. SSR). Zbl. Chir. 88(19):706-711, 1963.

Among 1122 pts. with gastric carcinomas, 29 gave a previous history of partial gastrectomy and 6 had undergone gastroenteroanastomosis (both groups, in the absence of any known malignancy). A careful study of these 35 cases, and of pertinent statistical data, confirmed that the surgery in question could not be considered an etiologic factor in subsequent development of cancer.

63-1189 THE RELATIONSHIP BETWEEN CHALCICOSIS AND PULMONARY CANCER IN ITS OCCURRENCE ON HOKKAIDO ISLAND. (Jap.) Aizawa, K. (Dept. Path. Hokkaido U. Sch. Med., Sapporo, Japan), K. Kikuchi, T. Kodama and T. Miyashita. Gan No Rinsho (Jap. J. Cancer Clin.) 9(3,4):139, 1963.

Among 40 cases of silicosis autopsied during the past 8 yr. in Hokkaido, 15 (37.5%) showed malignant tumors, including 6 of lung cancer. The av. age of the 6 lung cancer cases was 53 yr., clinical course lasted from several to 10 yr. (from onset to diagnosis), and occupational exposure ranged from 11-35 yr. (av. 22 yr.). In 96 autopsy cases of lung cancer in Hokkaido, 42 cases (43.8%) showed latent silicosis of the hilar lymph nodes of the lung; in 84 autopsies of non-cancerous cases, the rate was 16.6% (14 cases).

63-1190 CARCINOMATOUS DEGENERATION OF AN ULCER OF THE LEG. (Fr.) Bonnet, J., P. Téme, E. Calas, Y. Privat and F. Tasso. Bull. Soc. Franc. Derm. Syph. 70(1):118-119, 1963.

A 76-year-old Senegalese man was seen 14 yr. after extensive trauma to the right foot, which at the

time of first treatment, had healed except for a small ulcer which became aggravated by continuous irritation by the edge of the shoe. Biopsy revealed a proliferating hyperplasia of the epidermis without definite signs of malignancy. Local treatment for a period of weeks brought about improvement and the pt. was not seen again for 2 yr. at which time the ulcer had again progressed and degenerated to a well differentiated spinocellular carcinoma with regional lymph node metastases. Irradiation followed by cyclophosphamide (3 g i.v.) did not bring about improvement and the leg was amputated.

63-1191 DECLINE IN MORTALITY FROM GASTRIC CANCER IN NATIVE-BORN AND FOREIGN-BORN RESIDENTS OF NEW YORK CITY. (E.) Terris, M. (Div. Epidemiol., Publ. Health Res. Inst. New York City) and C. E. Hall. J. Nat. Cancer Inst. 31(1):155-162, 1963.

A decline in age-adjusted death rate from gastric cancer for the total population of New York City amounted to 31% for males and 39% for females for the period from 1949-1951 to 1959-1961. The mortality rates (per 100,000) for males, 1949-51 compared to 1959-61, for native-born white, foreign-born white, and Negro, were, resp.: 24.4 and 16.2 (-34%); 32.8 and 22.7 (-31%); 41.5 and 31.0 (-25%). Corresponding figures for females were: 13.1 and 7.2 (-45%); 19.8 and 13.1 (-34%); 22.2 and 15.7 (-29%). The decrease occurred in almost all age groups within each category, although it was less striking in the 80+ age group. From 1949-1951 to 1959-1961 the increase in proportion of those dying with operation and/or autopsy (an index of diagnostic accuracy) was identical in males and females, e.g., around +14%, with a greater increase in Negro males (+43%), foreign-born white females (+20%), and Negro females (+27%); the smallest increase was in native-born females (+5%). Since mortality rates decreased most in females and least in Negroes, improvement in diagnostic accuracy would not seem to be the answer. Instead the authors suggest that the decline is real, and due to unidentified environmental factors.

63-1192 CANCER OF THE BREAST: SOME OLD FACTS AND NEW PROSPECTIVES. (E.) Shimkin, M. B. (NCI, Bethesda). CA 13(3):109-112, 1963.

The maintenance of stable incidence, survival, and mortality rates in cancer of the breast suggests that the etiological, diagnostic, and therapeutic factors involved have remained either stationary or in a state of balance. Thus nonlactation nor the admin. of exogenous estrogens would appear to be important factors. Patients with breast cancer appear less likely to marry or marry late and have fewer children than comparable women of the general population. Cancer of the breast is more prevalent among sisters and daughters of these women and in addition they have more

dometrial but less cervical carcinoma. Extension of the study of breast cancer in Japanese men elsewhere than in Japan may provide leads to an understanding of the low incidence in this group. The finding of subnormal urinary excretion of 11-deoxy-17-oxosteroids in breast cancer pts. led to a prospective study on the island of Orkney, U.K. Potential value of blood specimens, for instance, collected from large populations and kept frozen, until index cases appear, is also discussed.

63-1193 SURGERY AND PROGNOSIS OF MALIGNANT NEOPLASMS. A STUDY BASED ON 3619 CASES. (E.) Tala, P. (Cent. Hosp., Helsingin Pitkätie-Helsingfors U., Finland), E. V. S. Lehtinen and P. Appelqvist. *Ann. Chir. Gynaec.* 52(123):1-90, 1963.

The present study is an analysis of 3619 malignant tumors seen between 1947-1956. Emphasis is placed on prognosis of surgical cases, and reference is made to the reports of Saxen in 1948, of Korpela *et al.* in 1961, and of Korpela, 1962 for incidence of various cancers in Finland. At the time of this study the incidence (per 100,000) of diagnosed cancers was 198, and the mortality rate was 144/100000. Only 56% of the cases analyzed were diagnosed histologically. The cancers of various sites (1) the number, (2) male:female ratio and (3) age group of highest incidence, resp., were: stomach, 939, 1.77, 50-69 yr.; lung, 657, 15.4, 50-59 yr. (49%); breast, 609, 40-59 yr. (61%); esophagus, 353, 50-69 yr.; gastric cardia, 185, 2.70, 50-59 yr.; rectum, 145, 0.75, 60-69 yr. (35%); colon, 117, approx. 1.00, 50-59 yr. (30%); urinary bladder, 109, 2.12, 60-69 yr. (38%); bone, 89, mean age 41 yr.; mediastinum, 104, 8, 40-69 yr. (60%); pancreas, 99, 2.12, 50-59 yr. (42%); prostate 87, 60-69 yr. (39%); kidney, 1.50, 40-69 yr. (82%); skin, 60, 1.00, 60-69 yr. (30%); thyroid, 60, 0.30, 60-69 yr.; salivary gland, 31, 0.73, 40-49 yr.; penis, 19, 50-59 yr.; testis, 19, all males, 53% over 60 yr., 5.3% under 60 yr.; testis, 10, 30-39 yr. (60%); small intestine, 9, 0.5, no ages given. The histologic type, when given was: small intestine, 5 carcinomas, 4 sarcomas; skin cancer, 45% melanoma, 45% epidermoid, 12% basal; mediastinum, lymphoma 60%; kidney, 42 hypernephromas, 1 epidermoid carcinoma; urinary bladder, 44% papillary; 96 verified, 40 osteosarcomas, 13, androsarcomas. The text discussion is amply supplemented by data from the above mentioned statistical studies in Finland.

63-1194 THE SUN FACTOR IN SKIN CANCER IN RHODE ISLAND AND NEARBY NEW ENGLAND. (E.) Winkler, M. (Miriam Hosp., Providence, Rhode Island). *Rhode Island Med. J.* 46(7):371 and 374, 1963.

Analysis of 400 biopsy-confirmed skin cancer cases

and of 400 noncancer controls showed the following frequencies, resp.: light eyes 67% and 41%; light skin 68.5% and 29.5%; easily sun-burned rather than tanned 71.5% and 29.5%; and males 66.0% and 47.8%. Among cancer pts. only 2.75% with light eyes, light skin, and inability to tan had minimal sun exposure, compared to 9.75% for the control series. Tumor type frequency in the present series was 82% basal cell carcinomas, 15% squamous, and 3% basosquamous, whereas in Southern states basal cell carcinomas had a frequency of 49-58%.

63-1195 MALIGNANT MELANOMAS OF THE UVEA IN DENMARK 1943-1952. A CLINICAL, HISTOPATHOLOGICAL, AND PROGNOSTIC STUDY. (E.) Jensen, O. A. *Acta Ophthal.* (Kobenhavn), Suppl. 75:220 pp., illus., 1963.

A historic review, including a review of histopathogenesis with special mention of pigmentogenesis, the mesoderm retinal and choroidal theories and a discussion of benign melanomas as the source of origin of malignant tumors, are presented. Of 100,918 malignant neoplasms occurring in Denmark between 1943-1952, 305 were malignant uveal melanomas, only 10 of which were melanomas of the iris. Etiological factors such as marital status, heredity, occupation, racial and geographic distribution, color of iris and hair, premorbid exposure to radioactivity, trauma, distribution between right and left eyes and duration are discussed. The series of malignant melanomas of the choroid and ciliary body showed a preponderance of males (56%), a highly significant preponderance of light iris colors, and a significantly more frequent occurrence (56%) of choroid and ciliary body melanomas of the right eye. Uveal malignant melanomas bore no relation to other diseases, general or local. Age of highest incidence for females was 50-59, for males, 60-69. There was no familial occurrence and no apparent relation to occupation or marital status. In the present series while 26 pts. (17%) had a history of trauma, it was concluded that it played no etiological role.

63-1196 64 CASES OF RETINAL GLIOMA OBSERVED IN VIET-NAM BETWEEN 1954 AND 1961. (Fr.) Nguyễn-Xuân-Nguyễn (Inst. Ophthalmol., Hanoi, Viet-Nam), Pan-Dân and Võ-Thê-Sao. *Med. Monde* 38(3-4):103-110, 1963.

In a Viet-Nameese family, 4/9 children developed retinal gliomata (bilateral in 1/4). Involved were the 2nd, 3rd, 7th and 8th children; a 5th child died of high fever and convulsions (etiology unknown) at the age of 8 mo. The report is supplemented by a discussion of 60 additional cases seen between 1954-1961; and by a review of statistics on the absolute incidence of the disorder, age of first appearance, symptomatology and complications, pathological classification, and treatment.

- 63-1197 PRECANCEROUS PHASES OF DEVELOPMENT AND MORPHOLOGY OF ACUTE TRAUMATIC SKIN EPITHELIOMA. (Rus.) Tolev, Iv. (Dept. Dermatol., Higher Inst. Med., Plovdiv, Bulgaria). *Folia Med.* 5(1):69-73, 1963.

Following the traumatic skin injuries 55/104 pts. developed skin epitheliomas immediately after injury; in 36/104 pts. in up to 1 yr.; 8/104 in up to 5 yr.; 5/104 in up to 10 or more yr. Histologically, 40 (38.45%) were spinocellular epitheliomas while 64 (61.55%) were basocellular. Macroscopically 53 were ulcerative, 11 were local infiltrates and 40 were nodular (1-2 cm. in diam.). As to site, 98% were in the head (99/104 face; 3/104 scalp), and 1% each in the upper extremities and sex organs. From data obtained the author found that the traumatic skin epitheliomas show a definite tendency for more rapid clinical development as compared with nontraumatic epitheliomas. The morphology of traumatic skin epithelioma in general does not differ substantially from that of epitheliomas of nontraumatic origin.

- 63-1198 BRONCHOGENIC CARCINOMA AND PULMONARY TUBERCULOSIS. (Fr.) Bariéty, M. and R. Rullière. *Rev. Tuberc. (Paris)* 27(1):1-10, 1963.

Among 250 pts. with bronchogenic carcinoma, pulmonary tuberculosis was demonstrable in 24 (9.6%); all were men between the ages of 44-76 (mean, 55). In 3 cases, the disorders were diagnosed simultaneously; in 20, the cancer occurred in pts. who had had TB; and in 1, TB was diagnosed in a pt. with an established carcinoma. In 3/24 cases, lesions of both types were found at the same site; in 18 more, they were found in close proximity in the same lung; and in 3, they occurred contralaterally. In 20/24 cases, the TB lesions were fibrotic and/or calcified. In 8 cases, a histologically confirmed anaplastic carcinoma was involved; in 12, an epidermoid carcinoma; and in 3/4 which could not be confirmed histologically, an epidermoid carcinoma was suggested.

- 63-1199 THE GEOGRAPHIC DISTRIBUTION OF CERVICAL CARCINOMA. (Ger.) Maass, H. (Gynec. Clin., U. Hamburg, Hamburg-Eppendorf, Germany) and H. Sachs. *Arch. Gynaek.* 198:619-623, 1963.

In a general statistical review, the author states that there is a markedly greater incidence of cervical carcinoma among groups in tropical regions (especially Africa and Asia), as compared to Europe and North America. Highest rates are in Central America and China. While the incidence of cervical carcinoma is only 2-4

times that of carcinoma of the corpus uteri in Europe, USA, and Australia, the relative frequency is much greater among Asiatic and African people, reaching as much as 50 times the incidence of corpus carcinoma in Djakarta, for example. Suggested possible contributory factors include the high birth rate in individual families, early age of marriage, unhygienic conditions among males, and the absence of the custom of circumcision.

- 63-1200 THE CAUSES OF THE HIGH CANCER MORTALITY IN THE POPULATION OF VIENNA WITH REMARKS ON A COMPARISON OF INTERNATIONAL STATISTICS ON CANCER DEATHS. (Ger.) Denk, W. (Aust. Inst. Cancer Res., Vienna). *Wien. Klin. Wschr.* 75(19):333-335, 1963.

Statistics of the years 1958 and 1959 show that the relatively high mortality (per 100,000) due to cancer in Austria (271.2 in 1959), and particular in Vienna (372.3) is due to a large extent to the precision of diagnosis of the causes of death, and to the high numbers of older people in the population. In other countries there were lower incidences, including the USA where the incidence was 157.9. The figures on mortality due to carcinoma of various organs show marked differences which are presumably due to different ways of life. A high mortality figure due to a particular carcinoma is usually partially compensated by a relatively low figure for another type of cancer. For instance, cancer of the respiratory apparatus accounted for 6.76% of the cancer deaths in men in Japan, 7.74% in Norway, 21.09% in the USA and 35.11% in Great Britain; cancers of the stomach on the other hand were, resp., 52.34%, 26.10%, 9.54%, and 15.31%. Detailed statistics are also given for Zurich and 3 cities in W. Germany.

- 63-1201 CARCINOMA OF THE BLADDER AND MULTIPLE UNRELATED MALIGNANCY. (E.) Ward-McQuaid, J. N. *Brit. J. Urol.* 35(2):169-172, 1963.

The incidence of association of other malignancies with carcinoma of the bladder is reported to comprise 5.4% of the total of bladder carcinomas reported to date when 180 new, consecutive bladder tumors (60% of which were histologically proven to be carcinomas) were added to 388 cases found in the literature. The frequency of various locations involved in such associations was: prostate, 22.1%; skin and lip, 12.4%; colon and rectum, 12.3%; bronchus, 9.6%; breast, 7.6%; uterus, 6.9%; stomach, 4.6%; renal adenocarcinoma 4.4%; reticuloses, 2.5%; pharynx and larynx, 2.5%; miscellaneous, 15.1%. The incidence is further analyzed as to age, sex, and the interval between the primary bladder tumor and diagnosis of the associated malignancy.

MISCELLANEOUS

63-1202 ENHANCING (XYZ) EFFECT IN INBRED MICE OF AUTOLOGOUS VERSUS ISOLOGOUS TUMOR.

(E.) Casey, J. G. (Birmingham Baptist Hosp., Birmingham, Ala.), H. J. Lohmann, C. W. Elliott and A. E. Casey. *Acta Un. Int. Cancr.* 19(1-2):128-131, 1963.

25 BALB/c mice pretreated with frozen and ycerinated JHA lymphatic leukemia tumors 3 wk. before JHA isografts, the 50% mortality point (MP) was 43 days compared with 52 days for controls given 4 serial passages where no male donor to female host transfers were made. Use of male donors in female hosts resulted in a significant but temporary enhancement in generations 2 and 29 of 7 and 9 days, resp. Significant permanent enhancement of 12 and 8 days occurred in generations 5-7 and 14-19, resp., and in each generation were preceded in generations 4 and 12-13 by only 2 significant inhibitions after male isografts of 13 and 20 days, resp. Enhancement of isologous XYZ antigens occurred in generation 4 of JHA already enhanced by 5 male donor to female host sequences. Enhancement occurred following male to female isografts in generations 4 and 5-7 of EL carcinosarcoma of the breast where the 50% MP was on day 30 for 16, and day 72, resp., compared to day 38 in generations 2-4 in 37 mice where males were not donors for females. The EL tumor enhanced in generation 4 was capable of still further enhancement (MP = 21 days in 20) when EL tumors retaining the original XYZ factor were used in generation 7. During generations 4-9, 50% MP was 23 days for 41 pretreated with frozen and ycerinated isologous XYZ from DX, MB, JHA, and EL tumors and 23 days for 44 untreated controls; 18 days for 12 pretreated with autologous isografts 3-4 wk. before inoc. with PC tumor.

63-1203 ON THE ENHANCEMENT OF THE GROWTH OF GUERIN RAT TUMOUR THROUGH ACTIVE IMMUNIZATION OF RATS WITH ANTIGENS OF MICE. (E.)

Wojewska, A. (Inst. Oncol., Dept. Tumor Biol., Warsaw, Poland) and K. Dux. *Acta Un. Int. Cancr.* 19(1-2):132-136, 1963.

In female rats preimmunized 24 hr. previously with normal C57Bl mouse antigens (0.5 ml of antigenate diluted 1:10 i.p.) were inoc. with a 1 ml suspension of the modified subline of rat lymphoma tumor T8C57a which had been passaged for three generations in rats, tumor takes occurred in 6/6 and av. tumor wt. was 7.2 g compared to nonimmunized controls, 6/6 and 4.5 g. In 2 similar experiments using the previously enhanced tumor cells in preimmunized rats, tumor takes occurred in 6/6 and 6/6, resp., and av. tumor wt. was 19.4 g and 10 g, resp., compared to controls with 2/12 takes and av. wt. of 4.5 g. It is assumed that the additional antigens in the modified Guerin subline are similar to or identical with antigens of mouse C57Bl antigens.

Immunological enhancement occurred in rats preimmunized with the antigens of normal mouse A2G tissue, rat tumor T8 and to a lesser degree with mouse BN/b. When female rats were preimmunized with normal mouse A2G antigens (i.p.) in five injections, 12, 9, 6, 3, and 1 day before tumor inoc., tumor takes occurred in 16/16 and av. tumor wt. was 6 g compared with rats preimmunized by two injections, 6 and 1 day before tumor inoc., 13/16 takes and 2.1 g av. wt. Preimmunization with 1 injection, 24 hr. before tumor inoc. was ineffective.

63-1204 RELATIONSHIP OF POLYDACTYLISM, TUMOR SUSCEPTIBILITY AND THE H-2 COMPLEX OF THE STRONG'S POLYDACTYLOUS DESCENTS IN MICE. (E., Abstract) Johnson, F. (Biol. Station, Roswell Park Mem. Inst., Springville, N.Y.), M. Flounders, H. Matsunaga and L. C. Strong. *Proc. Am. Assn. Cancer Res.* 4(1):32, 1963.

A relationship was found between the absence of polydactylia and susceptibility to a transplantable anaplastic carcinoma in Strong mice and their polydactylous descents. Genetic analysis suggests relation or linkage to the H-2 complex locus, with the pBr/St strain having the genotype H-2^x H-2^x. The incidence (percentage) of (1) polydactylism and (2) tumor susceptibility in the pBr/St mouse was 0 and 97.4; polydactylous sublines (poly 1, poly 2, poly 3, poly 4, and poly 5) results were, resp.: 80 and 10.7, 4 and 46.6, 60 and 0, 60 and 0 and 0.4 and 73.2. (See also CRA 1(1):#18, 1963.)

63-1205 CHROMOSOME ABNORMALITIES IN A MONGOL WITH ACUTE MYELOID LEUKEMIA. (E.)

Vincent, P. C. (Wellcome Lab. Exptl. Med. Surg., Royal North Shore Hosp., Crows Nest, England), S. Sinha, R. Neate, G. Den Dulk and B. Turner. *Lancet* 1:1328-1329, 1963.

A 2-year-old boy, the 4th child of a mother who had had 2 miscarriages, presented with acute myeloid leukemia of about 2 mo. duration, and died 7 wk. after admission. Autopsy confirmed the typical changes of mongolism, but no other congenital defects. Chromosome preparations from 5 different peripheral blood cultures revealed cells with 49 chromosomes in each sample, significantly more frequent in 3 (61.3%) than in 2 day (19%) cultures. All of 14 karyotypes prepared from cells with 49 chromosomes were identical and showed an abnormal pair of large metacentrics identical to pair 3 (Denver), an extra chromosome in the 6-12 group, monosomy in the 19-20 group, and trisomy 21. Karyotypes of cells with 47 chromosomes all showed trisomy 21.

63-1206 ATYPICAL PROLIFERATION OF EPITHELIUM IN HONEYCOMBED LUNG: INCIDENCE AND RELATION TO NEOPLASIA. (E., Abstract) Meyer, E. C.

and A. A. Liebow. Am. Rev. Resp. Dis. 88(1):126, 1963.

Among 153 pulmonary specimens resected for cancer, 21% showed honeycombing related to the tumor. When graded, the most extensive honeycombing occurred with slightly differentiated carcinomas, the least with highly differentiated epidermoid carcinomas. The group with honeycombing had a greater number of adenocarcinomas, and was all male. The incidence of cigarette smoking and prior pneumonias was significantly higher in the honeycombed group. In 403 controls from autopsies in pts. of the same age as the lung cancer group, 5% showed honeycombing, and one-fifth of these had concomitant carcinoma.

63-1207 SPONTANEOUS TRANSFORMATION IN CULTURED CELLS. (E., Abstract) Paul, J. (Dept. Biochem., U. Glasgow, Scotland). Proc. Roy. Soc. Med. 56(4):251, 1963.

A brief discussion of transformation in cell cultures, including a description of distinguishing features, such as altered phenotype, altered karyotype, and altered nutritional requirements. Although some authors have associated transformation with acquisition of malignant characteristics, the evidence does not suggest that a close relationship exists.

63-1208 GENETIC STUDY ON SUSCEPTIBILITY OF THE SOLID FORM OF LEUKEMIA OCCURRING IN THE C58 SUBSTRAIN MICE TO THEIR F₁ AND F₂ HYBRIDS. (Jap.) Kunika, A. (1st Dept. Intern. Med., Fukushima Med. Coll., Japan). Fukushima Igaku Zasshi (Fukushima Med. J.) 12(3):263-273, 1962.

A solid type of leukemia was serially transplantable in C58 mice. Transplants grew rapidly shortly after transplantation. Later, typical leukemia resulted with marked enlargement of liver, spleen and lymph nodes. The mice died in a cachectic condition due to their leukemia. When tumor-bearing C58 mice were crossed with normal CF1 or ddN strain mice, transplantability of the leukemia in the F₁ generations was 100%; in the second generation, transplantability of the C58 x CF1 was 83.3%, while that of C58 x ddN was 54.5%. Period until the appearance of leukocytosis was shorter in the F₁, but longer in the F₂ compared to the pure strain. Survival time of the tumor-bearing F₁ was shorter, that of F₂ longer.

63-1209 CANCER AND EXTRAVERSION. (E.) Coppen, A. (Med. Res. Coun., Neuro-

psychiat. Res. Unit, Carshalton, Surrey, England) and M. Metcalfe. Brit. Med. J. 1:18-19, 1963.

Extraversion (evaluated by responses to the Maudsley personality inventory questionnaire) was rated higher in 47 women who had developed cancer than in control groups of the same age from non-cancer hospital pts. (63) and another from the general population (31). This personality difference was highly significant in the case of breast cancer, but less significant in the case of non-genital cancer. The authors regard this difference as a manifestation of a constitutional deviation characterizing those women who had developed breast cancer.

63-1210 DEVELOPMENT OF CARCINOMA IN BLADDER DIVERTICULA. (Dut.) Karamat Ali, M. (Dept. Surg., U. Groningen, The Netherlands). Nederl. T. Geneesk. 107(26):1172-1176, 1963.

Supplementing a review of the literature, the author reports that 3/105 pts. with diverticula of the bladder (97 men, 8 women) also had primary diverticular carcinomas. All 3 occurred in the presence of obstruction of the bladder, due to prostatic hypertrophy. He concludes that such obstruction appears to be a major etiologic factor, and also appears to account for the fact that this malignancy is seen much more frequently in males (16 references).

62-1211 GENETIC STUDY OF MODIFIED SUSCEPTIBILITY TO TUMOR TRANSPLANTS IN RECIPROCAL RESISTANT BACKCROSS MICE. (E.) Sanford, B. H. (Roswell Park Mem. Inst., Buffalo). J. Nat. Cancer Inst. 31(1):169-178, 1963.

Striking differences in susceptibility to transplantation of the BST-2 mammary tumor (spontaneous in an A/St Strong female, transplanted for 106 generations) were noted in reciprocal backcross progeny involving 653 resistant mice from 4 matings: (C3HxA)F₁ female x C3H male, its reciprocal, and (AxC3H)F₁ female x C3H male, and its reciprocal. The offspring from the cross between (AxC3H)F₁ females and resistant C3H males developed significantly more tumors than did the progeny of resistant females crossed to F₁ males. There was also a significant difference between the offspring of reciprocal F₁ females. Lethal takes in backcross mice receiving transplants of tumor from F₁ passage were compared with takes in similar hosts receiving tumor serially transplanted only in A/St. Results suggest difference between the 4 backcrosses in response to a further variable influencing compatibility.

ERRATA:

1(5):#794, 1963: Lines 12-15, delete sentence starting "The plasma LDH response shows some conc. dependence..."

1(5):#919, 1963: Line 12, change 0.2 ml to 2 ml.

1(5):#937, 1963: Change first line of text to read: Fluorescent antibody studies of isolated ureteric buds,

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration(s)	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health, USA
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit(s)
e.g.	for example	ppm	parts per million
FFU	focus forming unit(s)	pt.(s)	patient(s)
g	gram(s)	RBC	red blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
ID ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution(s)
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit(s)
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose(s)	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukranian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

63-1212 GENERAL ETIOLOGY OF ENDOMETRIAL CANCER. (Sp.) Dexeus Font, S. Gynec. Serv., Provincial Maternity Inst. Barcelona, Spain), C. Carceller Blay, and Hierro Alberich. Tokoginec. Pract. 22(208):26, 1963.

A general discussion and review of the literature it is concluded that the determining factor in endometrial cancer is probably genetic, the actual carcinogenic factor is a profound hormonal disturbance. The hormonal factor appears more complex than simple hyperestrinism, may include pituitary hyperplasia and adrenal dysfunction. Clinical states which have been associated with endometrial cancer include uterine fibromyomas, hepatic insufficiency, and vitamin B deficiencies. The discussion includes data obtained in a series of 69 endometrial cancer cases, including a low frequency in women under 45 yr. (less than 2%), family history of cancer in 26.3%, and concurrent fibromyomas in 13.4%. (86 references)

63-1213 ON THE VIRAL ETIOLOGY OF CANCER. (E.) Zilber, L. A. (Gamaleya Inst. Epidemiol. Microbiol., Moscow). Acta Un. Int. Cancr. 1(2):219-227, 1963.

A review of his own work and that of others on the role of viruses in the origin of tumors, and the conclusions drawn follow. While some viruses convert normal cells into tumor cells, this transformation is hereditary and is aided by the additional genetic information brought by the virus into the cell. In the subsequent further development of the transformed cell, the virus does not play any significant role. It is possible that carcinogenic substances and factors do not act on the genome of cells but on the ways of transmission of genetic information blocked by corresponding repressor systems. Tumor viruses are widely spread in nature and can be present in the organism for a long time in a latent state. A number of factors contribute to the manifestation of pathogenicity. The former idea of strong species and tissue specificity of tumor viruses appears to be wrong, at least for some tumor viruses. The data obtained by the study of viral carcinogenesis has created a basis for the construction of a unified theory of the etiology of cancer into which many very controversial factors can now find their place. (54 references)

63-1214 CENTRAL AFRICAN LYMPHOMAS. (E.) Editorial. Lancet 2:23-26, 1963.

An editorial devoted to African lymphomas, is reviewed (15 references) the high incidence, presently limited geographic distribution, specific age distribution and characteristic

and unusual anatomical distribution particularly affecting the jaw bones. That there is a specific tumor promoting agent is suggested by the fact that, in Uganda, adult cases tend to be immigrants into affected areas from regions in which the disease was not seen in children. The possibility that the disease originates from spread of tumor alongside the maxillary artery and vein from an initial focus in the parotid glands may explain the location of early mandibular deposits, simultaneous involvement of the four quadrants of the jaw, and sparing of the mental region and may be relevant to the hypothesis that a virus is involved. (See also CRA 1(4):#740-743, 1963.)

63-1215 MEDICAL PROBLEMS CONNECTED WITH RADIOACTIVE FALLOUT. (Nor.) Eldjarn, L. T. Norsk. Laegeforen. 83(10):937-945, 1963.

The author surveys published data and recommendations on current and permissible levels of exposure to the various components of radioactive (Sr^{89} , Cs^{137}) fallout and the predictable immediate and remote effects of local fallout and accidental overexposure to radioactive particles. The author also emphasizes the danger of inducing subsequent cancers of the thyroid in children treated for thymic hypertrophy by X-irradiation of the neck or mediastinum. Because of the increase in the amount of I^{131} in radioactive fallout in recent yr., there is greater opportunity to accumulate sufficient radioactivity in the thyroid to induce subsequent neoplasm in pts. who receive I^{131} therapeutically or in tracer doses. (15 references)

63-1216 RIBONUCLEASE ACTIVITY AND CANCER: A REVIEW. (E.) Roth, J. S. (Inst. Cell. Biol., U. Connecticut, Storrs). Cancer Res. 23(5):657-666, 1963.

A review is presented of RNase activity in tumors, in sera of tumor-bearing animals, the effect of crystalline pancreatic RNase on tumors and tumor growth, and the relation of RNase activity to growth. In connection with RNase activity during carcinogenesis and in primary tumors induced by drug feeding, there appears to be fairly general agreement (in observations made mostly on liver) that there is a rise in specific activity of acid RNase, generally in the supernatant fraction. Changes in alkaline RNase are variable, depending on conditions. While in bacteria, plants, and some mammalian tissues, increased growth was associated with increased RNase activity, in a study of Walker 256 tumor in relation to protein intake, tumor RNase specific activity was inversely proportional to tumor size. (79 references)

63-1217 THE ROLE OF VIRUSES IN NEOPLASIA, WITH EMPHASIS ON HUMAN LEUKEMIA. (E.) Southam, C. M. (Sloan-Kettering Inst., N.Y.)

J. Pediat. 63(1):138-157, 1963.

An extensive review of the role of viruses in neoplasia is presented including their characteristics (course of infection, composition, transmission, masked infection, host range and pathogenic effects); clinical observations of the etiology of leukemia; and attempts to demonstrate human cancer viruses. Attempts to associate a virus with human leukemia are dealt with in detail. (150 references)

63-1218 HOST-TUMOR ANTAGONISM. XXXII. THE EPIDEMIOLOGY OF CANCER. (E.)

Pelner, L. (Swedish Hosp., Brooklyn, N.Y.). J. Am. Geriatr. Soc. 11(8):726-762, 1963.

Utilizing many published studies, cancers of various organs, notably the g.i. tract, uterus, penis, lung, prostate, breast, pancreas, thyroid, gallbladder, skin, esophagus, liver, and the group of lymphomatous diseases are reviewed and discussed at some length from the point of view of various etiologic relationships. Immunologic factors, i.e., lowered cancer rates for other organs after recovery from skin cancer are discussed as well as the criteria for identifying environmental agents as causes of cancer. (88 references)

63-1219 MAMMARY CARCINOGENESIS FROM METHYLCHOLANTHRENE. PART II. (It.)

Squartini, F. (Cancer Res. Div., U. Perugia, Italy) and M. Olivi. Lav. Anat. Pat. Perugia 23(1):97 pp., 1963.

A comprehensive analysis of the literature is presented, followed by tabulation of available data in order to obtain a complete picture of the various factors involved in mammary carcinogenesis from 20-methylcholanthrene (MC). After analysis of the effect of species, strains and crosses, routes and timing of MC admin., collateral treatments, etc., several experimental model systems, their characteristics and significance are discussed. It is concluded that in mammary carcinogenesis from MC, female sex hormones play a promoting role, and that the sequence of causal factors is important, as are the relative levels of hormones, the genetic make-up, and the frequency of spontaneous pseudopregnancies. In this respect the hormonal profiles of MC-induced and mammary tumor agent (MTA)-induced mammary tumors show little differences in mice. It is also noted that MC has a progesterone-like action. The literature contains discrepancies in results obtained from the same

strain, and at the present time these discrepancies are difficult to explain. (Approx. 90 references)

63-1220 ON SOME REGULAR RELATIONSHIPS BETWEEN CARCINOGENICITY OF AMINODIPHENYL DERIVATIVES AND THE STRUCTURE OF SUBSTANCE. (E.) Pliss, G. B. (Inst. Oncol., Acad. Med. Sci. USSR, Leningrad). Acta Un. Int. Cancr. 19(3-4):499-501, 1963.

The author reviews some of his own work and that of others relative to certain substitutions in the ortho position relative to the amino group. In rats, the carcinogenic effects of benzidine (E), N,N'-diacetobenzidine and a number of derivatives with different substitutions (OH, CH₃, OCH₃, OCH₂COOH, Cl, etc.) have been studied. Results support the conclusion that hydroxylation of B, or its transformation into benzidine diacetic acid reduces its carcinogenic activity. Methylation produced a similar change in carcinogenicity of B, while methoxylation resulted in marked decrease of carcinogenic effect. When chlorine had been introduced into the molecule, the carcinogenic effect was increased and modified, as shown by the development of skin tumors and its derivative bladder papillomas, etc. Substitution at the ortho position appears to inhibit hepatoma. Neither acetylation or methylation of B amino group has been found to inhibit the development of cirrhosis or hepatic tumors. The same trends were revealed with respect to effect of 4-aminodiphenyl derivatives on rats. In the ortho position to amino groups CH₃, OCH₃, OH, and Cl derivatives failed to induce liver tumors.

63-1221 DECANCERIGENIZATION OF SOME SHALE PROCESSING PRODUCTS. (E.) Bogovskii, P. (Inst. Exp. Clin. Med., Acad. Sci. USSR, Estonia SSR), G. M. Gortalum and A. V. Kozhevnikov. Acta Un. Int. Cancr. 19(3-4):481-482, 1963.

See CRA 1(3):#381, 1963.

63-1222 RELATIONSHIP OF VIRUS AND CELL IN EXPERIMENTAL LEUKAEMIA. (E.) Thorell, (Dept. Path., Karolinska Inst., Stockholm). Folia Biol. (Praha) 9(4):281-282, 1963.

A brief review and discussion of the formation and development of leukemia cells from virus-infected target cells in the hematopoietic organ of the mouse. Compared to normal cells, in leukemic cells there is an accumulation of cytoplasmic ribonucleoprotein. Also discussed is the ability of the leukemia virus to affect other types of target cells and the intracellular relationship between the virus and host. Several factors connect active virus with the nucleotide metabolism of the cytoplasm.

See also abstract no.: 1242

PHYSICAL CARCINOGENESIS

1223 CARCINOMA OF THE LUNG IN RATS EXPOSED TO THE β -RADIATION OF INTRABRONCHIAL THENIUM¹⁰⁶ PELLETS. I. DOSE-RESPONSE RELATIONSHIPS. (E.) Laskin, S. (Dept. Indust. Med. Univ., New York University Sch. Med.), M. Kushner, Nelson, B. Altshuler, J. H. Harley and Daniels. *J. Nat. Cancer Inst.* 31(2):219-231, 1963.

Groups of rats were exposed to β -radiation from thulium¹⁰⁶-plated pellets implanted in the bronchi. Levels varied from 0.008-13.6 μ C, and in terms of integrated dose from 10^3 - 10^6 rads. Since the spatial relationship of the emitting pellet to the bronchial origin of tumor was known, dose to the specific target tissue could be directly calculated. Of 265 animals exposed to the Ru¹⁰⁶, 68 developed squamous cell carcinomas of the bronchi; these occurred in dose-related fashion with incidence progressing from 0% in rats exposed to 10^3 rads to 65.6% in those exposed to 10^6 rads. No cancers were seen in 60 controls with platinum pellets or in 22 with sodium-plated pellets.

1224 COMPARATIVE LATE SOMATIC EFFECTS OF SOME RADIOMIMETIC AGENTS AND X-RAYS. (E.) Conklin, J. W. (Biol. Div., Oak Ridge Natl. Lab., Tenn.), A. C. Upton, K. W. Christenberry and T. P. McDonald. *Radiat. Res.* 19(1):156-168, 1963.

A number of 30-day survivors after admin. of X-rays (500-600 r), nitrogen mustard (HN₂; 3.7 or 4.5 mg/kg i.v.) or TEM (3.0, 3.5, or 4.0 mg/kg i.v.) to 1-week-old RF/Up female mice was: with X-rays, 259/360 (72%); with HN₂, 160/270 (59%); with TEM, 157/360 (44%); controls, 130/130; and their mean ages (in days) at death were: 396, 561, 508, resp.; controls, 638. The incidence of myeloid lymphomas and mean age (in days) at death of this tumor were, resp.: after treatment with HN₂, 3.7 mg/kg, 9% and 402; with HN₂, 4.5 mg/kg, 0% and -; with TEM, 16% and 360; with X-rays, 26% and 307; in controls, 5% and 605. Incidence of myeloid leukemia after treatment with HN₂, TEM, or X-ray was: 9%, 6%, and 7%, resp.; controls, 3%. Mean age (in days) at death with myeloid leukemia was: 511, 557 and 615, resp.; controls, 615. Reduced survival time was correlated with an increase in the X-ray-specific death rate from diseases of all types and not to the induction of neoplasia. Increased total incidence of pulmonary adenomas and lung tumors; HN₂, pulmonary adenomas and ovarian tumors; and X-rays, ovarian tumors, reduced the total incidence of pulmonary adenomas.

1225 EXPERIMENTAL DATA ON THE ROLE OF CHEMICAL MEDIATORS IN TUMOR GROWTH AND THE PRODUCTION OF THE RADIOBIOLOGIC EFFECT.

(Rum.) Grigorescu, S. (Inst. Oncol., Bucharest, Rumania), A. Trancu and I. Haulică. *Fiziol. Norm. Pat.* 7(4):265-274, 1961.

In experiments on albino rats irradiated with 325 r, admin. of epinephrine (0.1 mg i.p.) 5 min. before irradiation protected the animals against the leukopenic effect of X-ray treatment; on the other hand, admin. of this dose on days 3, 5, 6, and 7 after irradiation intensified the leukopenia. Acetylcholine (4 mg i.p.) 30 min. before irradiation increased its leukopenic effect; given after irradiation acetylcholine had no effect on the WBC response. In white rats with transplanted IOB 10 sarcoma, the repeated i.p. admin. of epinephrine (1 ml of a 0.002% soln.), started immediately or 20 days after transplantation, increased tumor take and stimulated the growth of established tumors. Acetylcholine (1 ml of a 0.5% solution), admin. under the same conditions, inhibited tumor take and growth. The radio-protective effect of epinephrine and its stimulating effect on tumor growth are attributed to its catabolic action, which was also reflected in wt. loss in treated animals. The accentuation of the leukopenic response to irradiation observed with prior admin. of acetylcholine is ascribed to its intensification of the adrenergic reaction to the stress of irradiation.

63-1226 MITOTIC ACTIVITY OF IONIZING RADIATIONS ON MALIGNANT AND BENIGN HYPERPLASIA OF THE MOUSE EPIDERMIS. III. COMMUNICATION: GENERAL SIGNIFICANCE OF PATHOLOGICAL MITOSES IN THE EPIDERMIS OF THE MOUSE. (Ger.) Setälä, K. (Inst. Path. Anat., U. Helsinki, Finland), B. Lindroos and O. Nyssönen. *Strahlentherapie* 121(1):97-114, 1963.

A more detailed description of the work abstracted in CRA 1(2):#200, 1963.

63-1227 THE EFFECT OF PROLONGED SOLAR RADIATION ON MELANOCYTES OF THE HUMAN EPIDERMIS. (E.) Mitchell, R. E. (Dept. Anat., U. Queensland, Australia). *J. Invest. Derm.* 41(4):199-212, 1963.

After examination of 76 samples of human skin from various parts of the body, giant dendritic melanocytes, giant spindle-shaped melanocytes and abnormal round adendritic melanocytes were found in skin exposed to prolonged solar radiation. Severe exposure resulted in the breaking up of the melanocyte dendrites and then of the cell body, and a reduction in the number of melanocytes in the epidermis. Similar changes were found in skin exposed to X-rays. The abnormal melanocytes did not appear to be able to transmit pigment to the epidermal cells. Melanocyte dendrites passing downward through the basement membrane have been described; and it is suggested that macrophages pass up to the basement membrane to receive the melanin directly.

63-1228 EFFECTS OF HEAVY HIGH ENERGY CHARGED PARTICLES. IV. THE FATE OF GIANT CELLS PRODUCED IN A NEOPLASM BY 20 MEV DEUTERON BOMBARDMENT. (E.) Lippincott, S. W. (Bowman Gray Sch. Med., Winston-Salem, N.C.), W. G. Galvo, C. P. Baker, J. E. Jesseph, C. R. Jansen and L. E. Farr. Arch. Path. (Chicago) 76(5): 543-552, 1963.

Giant neoplastic cells were produced in Sarcoma 37 transplants in mice by irradiation with 20 mev deuterons. Both *in vitro* irradiation prior to implantation and *in situ* irradiation of viable neoplasm after implantation gave rise to the same type of giant neoplastic cells. Histological study at daily intervals revealed that the neoplastic cells did not reproduce themselves.

63-1229 EXPERIMENTAL LUNG CANCER INDUCED WITH RADIOACTIVE COMPOUNDS P³², Au¹⁹⁸ AND Fe⁵⁹. (E.) Kochetkova, T. A. (Inst. Indust. Hygiene Occup. Dis., Acad. Med. Sci. USSR, Moscow), G. A. Avrunina and N. D. Sagaidak-Chernyak. Acta Un. Int. Cancr. 19(3-4):684-686, 1963.

Lung changes in white rats were studied after the intratracheal inj. of radioactive substances. Injection of Fe⁵⁹2O₃ (1-27 μ C x l; total dose 500-10,000 rads) induced lung cancer in 8/52, over a period of 6-9 mo. exposure. Injection of CrP³²O₄ (40-100 μ C doses; total 1,300-15,000 rads) induced lung cancer in 11/76 after a period of irradiation of 6.5-18 mo. After Au¹⁹⁸ (colloidal, 100-150 μ C doses; total 5,400-8,000 rads) incidence was 3/30 over a period of 2.5-12 mo. Na²⁴Cl inj. one to many times in doses of 100-2,100 μ C did not cause lung cancer.

63-1230 EXPERIMENTAL RHABDOMYOBlastomata AND THEIR IMPORTANCE FOR AN ANALYSIS OF THE PHENOMENA OF TUMOROUS TRANSFORMATION. (E.) Studitskii, A. N. (A.N. Severtsov Inst. Anim. Morphol., Acad. Sci. USSR, Moscow). Acta Un. Int. Cancr. 19(3-4):648-651, 1963.

See CRA 1(4):#617, 1963.

63-1231 STUDIES IN SUBCUTANEOUS CARCINOGENESIS WITH IMPLANTS OF GLASS AND TEFLON IN MICE. (E.) Tomatis, L. (Div. Oncol., Chicago Sch. Med., Ill.). Acta Un. Int. Cancr. 19(3-4): 607-611, 1963.

Swiss albino mice have been implanted s.c. with pieces of teflon and glass of different shapes

and sizes. Implantation of square pieces of glass and teflon of the same size (12 mm) gave rise to similar incidences of tumors (13.6% and 10%, resp.). Glass fragments yielded 4% tumors. Teflon discs (15 mm) gave rise to 22.7% tumors; similar discs 2 mm in diameter yielded 15.2% tumors. Larger teflon discs (20 mm) in female and male mice yielded 15.2% and 8.0% tumors, resp. Teflon fragments gave a tumor incidence of 21%. The presence of a continuous surface of the implant does not appear to be a vital factor. The implantation of glass combined with admin. of trypan blue resulted in a lower tumor incidence than obtained with glass alone. The implantation of glass or teflon combined with the admin. of urethan did not shorten the latent period of the tumors induced by implants.

63-1232 COMPARISON OF MAMMARY NEOPLASIA IN THE RAT INDUCED BY CHEMICAL PLUS PHYSICAL CARCINOGENS. (E.) Shellabarger, C. J. (Zool. Dept., U. Michigan, Ann Arbor). Acta Un. Int. Cancr. 19(3-4):799-801, 1963.

When 244 r of total body X-ray exposure was added to 5 daily doses of 5 mg of 20-methylcholanthrene (20-Me), the capacity of X-rays to induce fibro-adenomas and adenofibromas in rats was not impaired. However, the addition of X-ray exposure to 20-Me did not enhance the carcinogenic potential of 20-Me, in fact the combined treatment may have produced fewer adenocarcinomas than 20-Me alone.

63-1233 SEMI-QUANTITATIVE RELATIONSHIP OF RADIATION AND NEOPLASIA IN MAN. (E.) Archer, V. E. (P.O. Box 2539, Fort Douglas Station Salt Lake City, Utah) and C. L. Simpson. Health Phys. 9(1):45-56, 1963.

The hypothesis that a linear relationship exists between dose and induction of neoplasms is supported by data for humans. This hypothesis involves the use of dosage in gram rad applied to organs or body sections of a group of individuals. It permits the calculation of various integral doses required to produce one neoplasm "on the average". Infants and children are shown to be more prone to radiation-induced neoplasia than adults. The integral dose to reticuloendothelial tissues of children requires about 4×10^6 g rad to produce one leukemia. This contrasts with about 180×10^6 g rad required to produce one leukemia in adults. The integral dose required to produce cancer other than leukemia is about 16×10^6 g rad for children and about 180×10^6 g rad for adults. Application of these values to assessment of radiation hazard are suggested.

See also abstract nos.: 1215, 1314, 1331, 1343, 1374

CHEMICAL CARCINOGENESIS

-1234 THE N- AND RING-HYDROXYLATION OF 2-ACETYLAMINOFLUORENE AND THE FAILURE TO DETECT N-ACETYLATION OF 2-AMINOFLUORENE IN THE URINE. (E.) Poirier, L. A. (McArdle Mem. Lab. Cancer Res., U. Wisconsin Sch. Med., Madison), A. Miller and E. C. Miller. Cancer Res. 23(5):790-800, 1963.

After ingestion of 2-acetylaminofluorene (AAF) and N-hydroxy-AAF by male dogs, both compounds were recovered in the urine, but not 1-, 3-, or 4-hydroxy-AAF. These metabolites were not found in the urine when dogs were fed 2-aminofluorene (AMF), N-hydroxy-2-AMF, 1-hydroxy-AAF, or 4-hydroxy-AAF. Dietary supplementation with calcium pantothenate and riboflavin and an attempt to induce acetylase activity by feeding 2-AMF for several days did not lead to the urinary excretion of any recognizable acetylated urinary metabolites of 2-AMF. Under similar conditions the specific activities of the acetylated urinary metabolites of 2-(acetyl-1¹⁴C)-AMF fed in mixtures with unlabeled 2-AMF were not appreciably different from the specific activity of the ingested acetyl-labeled AAF. N-hydroxy amides were detected in the urine of dogs after ingestion of the following amides: acetanilide and its p-vinyl, p-fluoro, and p-hydroxy derivatives; trans 4-acetylaminostilbene; propionylaminofluorene; and 2-n-butylaminofluorene. Administration of 2-acetylaminophthalene to a dog led to urinary excretion of very small amounts of this amide and its N-hydroxy metabolite. Synthesis of N-hydroxy-2-AAF is described.

-1235 CANCEROGENIC SUBSTANCES IN WATER. (Ger.) Borneff, J. (Inst. Hygiene, Johannes Gutenberg-U., Mainz, Germany). Münschen Wschr. 105(24):1237-1242, 1963.

Brief presentation of a study of polyaromatic hydrocarbons in various surface waters (see Abstracts 1(3):#412, 1963) but with more discussion of possible origin of this material, such as in weeds, soils, debris from asphalt highways and endogenous production in plants.

-1236 REGENERATION AND CANCER FORMATION IN LIVER PARENCHYMA. (Ger.) Oehlert, W. in. Wschr. 41(10):520-521, 1963.

Discussion of liver parenchyma transformation based on work previously abstracted in CRA Abstracts 4(4):#660, 1963.

-1237 FURTHER STUDIES ON METHYLCHOLANTHRENE-INDUCED TUMOURS OF THE GALLBLADDER AND LIVER IN THE GOLDEN HAMSTER. (E.) Bain, G. O. (Dept. Path., U. Alberta, Canada), J. Siegenberg and K. Kowalewski. Canad. J. Surg. 6(3):367-371, 1963.

Golden hamsters fed a high cholesterol diet (addition of 2% cholesterol and 5% olive oil to basal diet) developed fatty livers and a high incidence of cirrhotic changes. In such animals the incidence of gallbladder carcinomas 53-407 days after intracholecystic implantation of 20-methylcholanthrene (20-Me) pellets (as previously described) was 83% in 24 animals, compared to 57% of 14 controls. After intrahepatic implantation of 20-Me pellets to hamsters on control or high cholesterol diet, few tumors were induced (20% and 25%, resp.) and these were of the 20-Me-sarcoma type.

63-1238 ADENOCARCINOMA IN THE LUNGS OF MICE EXPOSED TO VAPORS OF 3-NITRO-3-HEXENE. (E.) Deichmann, W. B. (Dept. Pharm. Path., U. Miami Sch. Med., Coral Gables, Fla.), W. E. MacDonald, W. A. D. Anderson, and E. Bernal. Toxic. Appl. Pharmacol. 5(4):445-456, 1963.

Groups of male and female Swiss Webster mice were exposed to the vapor of 3-nitro-3-hexene (0.2 ppm, 6 hr./day x 5/wk.): 10 in a chamber at 49% relative humidity; 10 at 90% relative humidity. Among those which survived from 128-302 exposures (over 439 days) 5 developed adenocarcinomas of the lung: 4 in those exposed to 49% humidity and 1 among those exposed to 90% humidity. Among 2 similar groups of controls kept under the same conditions of humidity but without exposure to the nitro-olefin, 1 developed an adenoma of the lung. In the experimental animals signs of irritation were minimal. Fatalities were about equal in both groups. Most of the early deaths encountered were from fighting, and possibly because of a bacterial infection.

63-1239 RELATIONSHIP BETWEEN HOST RANGE AND ISOANTIGENIC PROPERTIES IN DIFFERENT SUBLINES OF THE SAME SARCOMA. (E.) Klein, E. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm, Sweden) and E. Möller. J. Nat. Cancer Inst. 31(2):347-364, 1963.

Sarcoma MCAG, induced with 20-methylcholanthrene in an (A x A.CA)F₁ hybrid mouse, and sublines with different host range were studied with regard to H-2 isoantigens. Cells of the original F₁ tumor proved asymmetric for the 2 parental isoantigen complexes -- they appeared to contain more H-2^f than H-2^a. After inoc. of these cells, A.CA mice produced anti-H-2^a antibodies earlier than A mice responded with anti-H-2^f antibodies. The transplantation behavior of the tumor was explainable on the basis of these findings. A variant subline showing strict transplantation specificity toward the parental strain A had lost the H-2 antigens derived from the A.CA parental genotype and had a considerably increased conc. of the remaining H-2^a antigen complex. The loss of specificity was accompanied by decrease in amount of H-2 antigens on the cells.

- 63-1240 THE ANTHRATEROID REARRANGEMENT. XI. THE CONVERSION OF $\Delta^{5,7,9}$ -ANTHRA-PREG-NATRIEN-20-ONE TO 4',10-DIMETHYL-1,2-BENZANTHRA-CENE BY A MODEL OF A BIOCHEMICAL ROUTE. (E.) Nes, W. R. (Dept. Chem., Clark U., Worcester, Mass.) and D. L. Ford. *J. Am. Chem. Soc.* 85(14): 2137-2141, 1963.

$\Delta^{5,7,9}$ -Anthrapregnatrien-20-one, after 17 α -hydroxylation was converted via the D-homosteroid rearrangement and dehydrogenation to 4',10-dimethyl-1,2-benzanthracene. The latter compound was found to be identical with a sample prepared by total synthesis. The major conversions leading from the anthrasteroid structure to the benzanthracene structure were found to parallel known types of biochemical reactions, and these or related reaction sequences are suggested as possible routes for the biochemical formation of a carcinogen.

- 63-1241 HEPATIC TUMORS INDUCED BY SELENIUM. (E.) Cherkes, L. A. (Lab. Path. Physiol., Inst. Nutr. AMN USSR, Moscow), S. G. Aptekar and M. N. Volgarev. *Biull. Eksp. Biol. Med. (Eng.)* 53(3):313-317, 1963.

Sodium selenate (10 mg/kg food) was fed to 40 heterozygotic male rats (which are less sensitive to selenium than females). Of 23 rats which survived for over 18 mo., tumors developed in 7: 3 carcinomas of the liver (with metastases to the lungs in 2 cases), and 4 sarcomas. Adenomas of the liver parenchyma were found in 3 rats. Addition of riboflavin to the diet (10 mg/day), beginning at the 7th mo., did not change the pathological process. The appearance of the liver of 4/13 rats which did not develop tumors was judged to be somewhat similar to what is found in the early stages of the reaction to various carcinogens, or to the inclusion of ethionine in the food. In 9 rats the liver changes were typical of the usual chronic selenium poisoning.

- 63-1242 POLYCYCLIC AROMATIC HYDROCARBONS, THEIR ANALOGUES AND DERIVATIVES, AS POTENTIAL PHARMACOLOGICAL AGENTS. (E.) Buu-Hoi, N. P. (Natl. Ctr. Sci. Res., Paris). *Med. Exp. (Basel)* 8(4-6):209-217, 1963.

The author reviews the earlier use of carcinogenic polycyclic hydrocarbons such as 3,4-benzpyrene, 9,10-dimethyl-1,2-benzanthracene, and 20-methyl-cholanthrene (20-Me) as cancer chemotherapeutic agents. Substances whose tumor growth inhibiting activity do not correspond with their carcinogenicity include the angular benzophenothiazines and dibenzophenothiazines which are noncarcinogenic inhibitors of Walker carcinoma 256 in rats; 1,2:5,6-dibenzofluorene which possesses considerable inhibitory activity; and the non-carcinogenic naphth-2',1':1,2-anthracene. 11,12-Benzofluoranthene has been found to be sarcomogenic. In a presentation of his own research, the author mentions that 6-aminochrysene inhibited

skin carcinogenesis induced by 20-Me and of spontaneous mammary adenocarcinomas in mice.

- 63-1243 ISOLOGOUS PITUITARY IMPLANTS IN THE KIDNEY OF GOLDEN HAMSTERS. (It.) Della Porta, G. (Natl. Cancer Inst. Milan, Italy). *Tumori* 49(2):139-146, 1962.

Single isologous pituitary grafts (under the renal capsule) to 7-12-week-old females of either of two highly inbred substrains (GHM or CDM) gave identical results whether from sisters or brothers father, or non-litter mate males. Successful grafts were obtained in 18/19 animals. All the grafted females showed diffuse acinar hyperplasia of the mammary gland, often accompanied by milk secretion, ductal hyperplasia and ectasia, but no mammary tumors. Ovaries of grafted animals showed normal follicular cycles, with slight stromal hyperplasia and luteinization. Four tumors (an undifferentiated sarcoma of the limb metastatic to the spleen, 1 angioma of the spleen, 1 cecal polyp, and 1 colon polyp) were observed in grafted animals, and also in the CDM substrain, frequent fibrotic lesions of the liver, but none were thought to be related to grafting. Results indicate that isologous pituitary grafts in golden hamster females stimulate production of sufficient prolactin to affect the mammary gland, but do not induce mammary tumors.

- 63-1244 MODERN FILTER CIGARETTES AND THEIR EFFECTS ON SMOKING HABITS AND ON SMOKE INHALANT SUBSTANCES. (Ger.) Waltz, P. (Fabriques de Tabacs Reunies SA, Neuchatel-Serrieres, Switzerland) and M. Häusermann. *Zschr. Praeventivmed.* 8(2):73-98, 1963.

Cigarettes made with chemically different cigarette papers, when smoked on the electrostatic smoking machine, showed condensate reductions of about 10%; high porosity paper reduced it another 5%. Efficient filters reduced total condensates by an av. of 33%. Use of low nicotine content tobacco reduced smoke condensate by 18% and the nicotine by 36%. The cumulative reductions amount to about 50%. Specific substances can also be reduced: thus by a change to non-arsenical insecticides, As₂O₃ content was reduced from 56.5 ppm in 1951 to 2.7-14.4 ppm in 1958. In 4 brands, the filters retained phenols to the extent of 60-92%. For 3,4-benzpyrene, filter effectiveness paralleled that for the total condensate. In the U.S., mean smoke condensate per person per year dropped from 77.74 g in 1957 to 61.96 g in 1961. Since mean butt length has increased between 1955 and 1962, an estimated reduction of 1.6 puffs/cigarette reduced total smoke condensates by 19%. Since data on individual smoking patterns showed no real difference in amounts inhaled, smokers do not compensate for filtration by more inhalation. (See also CRA 1(6): #1079; and *ibid.*, #1093, 1963.)

- 63-1245 EFFECT OF SEX AND CASTRATION ON THE INDUCTION OF MUSCLE TUMORS IN THE RAT BY

CKEL SULFIDE. (Fr.) Jasmin, G. (Dept. Pathol. at., U. Montreal, Canada), E. Bajusz and Mongeau. Rev. Canad. Biol. 22(1):113-114, 1963.

experiments on intact rats of both sexes and strated males, nickel sulfide was inj. into e gastrocnemius muscle and the number of abdomyosarcomas produced in the various groups s compared. Tumor production was much more equent in intact females (50% of 14) than in tact males (30% of 10) and was least frequent 0% of 10) in castrated males; also, the tumors re larger (8.2 g) in intact females than in tact males (4.7 g) or male castrates (4.4 g). ne of the tumors in the castrates metastasized the lymph nodes, as compared to 4/14 of those females and 1/10 in intact males. While 50% the intact males had died or been killed be- use of pulmonary disease by the end of the 182- y observation period, the authors doubt that les are actually more susceptible to the carci- genic action of nickel. Their previous finding at the anabolic and myotrophic hormone, methan- ostenolone, increases the incidence and accel- erates the development of experimental rhabdo- sarcoma is accounted for by the stimulating fect of this hormone on skeletal muscle fiber abolism.

-1246 VARIOUS TYPES OF NUCLEI IN THE LIVER PARENCHYMA OF THE RAT DURING CARCI- GENESIS. (Fr.) Daoust, R. (Montreal Cancer st., Canada). Rev. Canad. Biol. 22(1):59-71, 1963.

medial and lateral liver lobules of normal ult male Wistar rats, periodic examination of e nuclear volume (determined according to rcrombie) showed 3 mean peaks at 171, 336, 652 μ^3) or a geometric progression of 1:2:4 responding to diploid, tetraploid, and aploid nuclei. Over a period of observation 180 days, there was a relative decrease in oid and increase in tetraploid nuclei. Rats a low protein diet + dimethylaminoazobenzene B; 0.06% x 180 days p.o.) showed an appreciable ber of large, i.e., highly polyploid nuclei both normal and tumor tissue. The parenchyma hepatoma tissue differed from non-cancerous sue by showing no distinct nuclear classes, bably because of the formation of an appreci- e number of aneuploid cells during tumor elopment. (See also CRA 1(5):#843, 1963.)

1247 INHIBITORY EFFECT OF 3-METHYLCHOLAN- THRENE ON INDUCTION OF MASSIVE NECROSIS ADRENAL CORTEX BY 7,12-DIMETHYLBENZ(a)ANTHRA- E. (E.) Dao, T. L. (Roswell Park Mem. Inst., falo) and Y. Tanaka. Proc. Soc. Exp. Biol. 113(1):78-81, 1963.

cessive feeding of 20-methylcholanthrene (20- 30 mg/day x 2) 48 hr. before admin. of

9,10-dimethyl-1,2-benzanthracene (DMBA; 20 or 30 mg x 1) inhibited completely the necrosis- inducing action of DMBA on the adrenal glands. The adrenal cortex in rats receiving 20-Me prior to DMBA treatment appeared histologically normal. This protective effect was also observed in rats pretreated with Metopirone, a compound known to suppress adrenal corticosterone synthesis by inhibition of 11β -hydroxylation. The mechanism by which 20-Me inhibited the necrosis-inducing action of DMBA was believed to be similar to that by which Metopirone inhibited it.

63-1248 THE MITOGENIC PROPERTY OF PHYTOHAEMAG- GLUTININ: STUDIES ON HUMAN LEUCOCYTES. (E.) Elves, M. W. (Dept. Clin. Hemat., U. Royal Infirmary, Manchester, England) and M. C. G. Israels. Brit. J. Haemat. 9(3):407-411, 1963.

In experiments performed on human lymphocytes, it was shown that the agglutinating and mitogenic properties of phytohemagglutinin (PHA) were closely bound together. Cells in culture did not take up PHA from the medium. The lymphocyte transformation due to PHA was inhibited in the presence of prednisolone. The lymphocyte response was greater to PHA(P), a highly purified prepara- tion, than to PHA(M), which is a relatively crude bean extract which has been shown to con- sist of a protein fraction and a mucopolysaccharide fraction. The hypothesis is advanced that the lymphocyte transformation observed when these cells are cultured under the influence of PHA is an antigen-antibody-like response of the cells to PHA.

63-1249 ENDEMIC PNEUMONIA VIRUS ISOLATED FROM MALIGNANT LYMPHOMA INDUCED IN SWISS MICE BY 9,10-DIMETHYL-1,2-BENZANTHRACENE. (E.) Bather, R. (Saskatchewan Res. Unit, Natl. Cancer Inst., Canada) and J. Cushing. Cancer Res. 23(5): 707-713, 1963.

See CRA 1(5):#833, 1963.

63-1250 NUCLEIC ACID CONTENT OF RAT LIVER DURING CARCINOGENESIS. (Uk.) Rubenchyk, B. L. (Ukraine Inst. Nutr., Kiev, USSR). Ukr. Biochem. Zh. 35(3):352-355, 1963.

Liver tumors were induced in white rats (150-200 g), by feeding them p-dimethylaminoazobenzene (DAB, 0.06%) for about 4 mo. or thioacetamide (TAA; 0.2%) for about 6 mo. Six wk. after in- itiation of treatment, the conc. of liver DNA progressively increased to reach a max. at wk. 20-26, while the conc. of RNA remained unaltered or was slightly decreased on wk. 2 after DAB, and on wk. 6 after TAA. The ratio of RNA to DNA, 2 wk. after the initiation of treatment was 3.2 and 3.3, resp., as compared to 1.83 and 1.9, resp., while the tumor was developing. In untreated controls the RNA to DNA ratio changed from 4.1 to 3.4 at the end of the period of observation.

- 63-1251 CHEMOTHERAPY EXPERIMENTS WITH HEPATOMAS. (Ger.) Schmäh, D. (Inst. Path., Rheinische Friedrich-Wilhelms U., Bonn, Germany), G. Schrick and K. König. Arzneimittelforschung 13(5):370-371, 1963.

The hepatomas induced in rats by feeding either diethylnitrosamine or dimethylaminoazobenzene, or a combination of both (dose and duration not specified) showed no therapeutic response to treatment by cyclophosphamide or Trenimon (each about 30% of the LD₅₀).

- 63-1252 STUDIES ON AZO-DYE CARCINOGENESIS IN RAT LIVER. THE EFFECT OF 4-DIMETHYL-AMINO-3'-METHYLAZOBENZENE ON THE INCORPORATION OF (¹⁴C)LEUCINE INTO RAT-LIVER MICROSOMAL PROTEIN. (E.) Hawtrey, A. O. (South African Council Sci. Indust. Res., Pretoria). Biochem. J. 88(1): 106-114, 1963.

After a single inj. of 4-dimethylamino-3'-methylazobenzene (DMeAB; 200 mg/kg) into female rats (200-250 g), incorporation of leucine-C¹⁴ into protein by a system of washed microsomes plus pH 5 enzyme showed increase in rate and increase in specific activity of the microsomes after 20 hr., reaching a max. at 40 hr. with subsequent return to normal. Maximum binding of dye to microsomes, pH 5 enzymes and pH 5 supernatant was maximal after 40 hr. The incorporation of leucine-C¹⁴ into the microsomal protein of mitochondrial supernatants was considerably inhibited 4 hr. after admin. of dye, with a return to normal after this time. A diffusible inhibitor of the incorporation of leucine-C¹⁴ was found in both normal pH 5 supernatant and 'azo'-pH 5 supernatant. The 'azo'-microsomal incorporating system was affected by both supernatant fractions to a much greater extent than was the normal microsomal incorporating system. Fractionation of the pH 5 supernatant of homogenates from azo-dye-treated rats with ammonium sulfate gave 3 fractions that all stimulated the incorporation of leucine-C¹⁴ and were also able to replace the pH 5-enzyme fraction to a certain extent.

- 63-1253 EXPERIMENTAL TUMORS ORIGINATING IN MUSCLE TISSUE. (Georgian, Russian Summary) Georgadze, G. G. Tr. Inst. Eksp. i. Klin. Khir. i Gematol., Akad. Nauk Gruz.SSR 10:261-275, 1962.

When hamsters (Mesocricetus brandti) are given i.m. inj. of 9,10-dimethyl-1,2-benzanthracene (2 mg in benzene) into the hip, the benzene (unlike butter or vegetable oils) is not encapsulated, permitting direct contact of the carcinogen with the tissues. A histological study of the changes in the muscle tissue following inj. of this type showed that polymorphocellular and giant cell polymorphous sarcomas, as well as most spindle cell sarcomas, arise in striated muscle tissue.

- 63-1254 HIGH SUSCEPTIBILITY OF MICE WITH ALLOXAN INDUCED DIABETES TO THIO-TEPA, A TERATOGENIC AGENT. (Jap.) Takano, K. (Kyoto U. Sch. Med., Japan) and H. Nishimura. Kaibogaku Zasshi (Acta Anat. Nippon) 38(1):45-46, 1963.

After induction of diabetes in 3-4-month-old dd strain pregnant mice by admin. of alloxan (0.2 mg/g i.p.) on pregnancy days 8-9, thio-tepa (2.5 µg/g) was given on days 10-11. As a result, more severe types of deformities (defects of toes, polydactylia, harelip, etc.) and a higher incidence (47%) were found in fetuses from diabetic mice than among fetuses from control animals (16%).

- 63-1255 THE EFFECTS OF TRIAMCINOLONE DIACETATE ON LEVELS OF 3-METHYLCHOLANTHRENE IN RAT MAMMARY GLANDS. (E.) Bolasny, B. L. (Dept. Surg., U. Chicago Sch. Med., Ill.), S. E. Warren and J. V. Prohaska. Cancer Res. 23(7):971-973, 1963.

The suppression of 20-methylcholanthrene (20-Me)-induced mammary carcinoma in the white rat produced by triamcinolone diacetate (TR) was investigated by the quantitative analysis of the localization of 20-Me in the mammary gland of rats receiving TR as compared with rats not receiving this steroid. The analysis shows that there is no difference in the uptake of 20-Me in rats receiving TR. Levels of 20-Me in the mammary gland increase in direct proportion to the quantity of carcinogen fed. A single oral dose of 20-Me (50 mg) disappears from the breast in 15 days in normal, as well as in TR-treated rats. The results indicate that the suppression of mammary carcinoma produced by TR cannot be explained by the altered uptake or clearance of carcinogen by the mammary gland.

- 63-1256 THE DYNAMICS OF ROENTGENOLOGICAL CHANGES IN THE RABBIT UPPER JAW DURING THE DEVELOPMENT AND GROWTH OF INDUCED TUMORS. (Rus.) Mel'nikov, R. A. (Inst. Oncol., Acad. Med. Sci. USSR, Moscow) and A. F. Kondrat'eva. Vop. Onkol. 9(7):21-32, 1963.

Repeated X-ray examinations were carried out in rabbits after inj. into the maxillary bone of 20-methylcholanthrene (15-50 mg) or 9,10-dimethyl-1,2-benzanthracene (8-10 mg) in groups of 51 and 17 animals, resp. Malignant tumors of the maxilla appeared in 32/68 from 155-850 days after inj. Early roentgenological changes in some of the tumors included loss of the reticulum of the bone a change in the sharpness of the cortical walls of the jaw, with a moderate protrusion in one case. There was also enlargement of the upper jaw which showed small areas of sclerosis with indefinite borders. In the study of the dynamics of the development of tumor in the maxilla, X-ray examination revealed the following types and forms of growth: osteolytic, osteoblastic (and a mixture of these 2 forms), and also a diffuse form of sarcoma.

257 THE STIMULATING EFFECT OF TEZAN AND PENTOXYL ON THE GROWTH OF TRANSPLANTABLE RS. (Rus.) Chernichenko, V. A. (Dept. tgenol., Kiev Postgrad. Med. Inst., USSR) N. M. Kralich. Vop. Onkol. 9(7):41-44, 1963.

ps of 20 random bred male mice (18-20 g), ys after s.c. inoc. of Ehrlich ascites tumor, treated with tezan-25 (T; 0.4 mg/kg x 10,) or pentoxyl (5-hydroxymethyl-4-methyluracil, 0 mg/kg x 10, s.c.). The av. tumor wt. in receiving T was 441 (mg?), in mice receiving 87, controls 187. Survival times (days) was 20 and 27, resp. The authors conclude that use of hematopoietic stimulators in oncolog- practice to prevent leukopenia is unwise e they stimulate the growth of any cells, only blood cells.

258 SNUFF LESIONS OF THE ORAL CAVITY: A CLINICOPATHOLOGIC STUDY OF FORTY-EIGHT S. (E.) Palileo, L. G. (Lab. Serv.; Quezon ., Quezon City, Philippines), J. L. Smith, Jr., . MacComb and S. Soriano, Jr. Bull. Quezon . 6(4):119-123, 1962.

g 150 pts. observed from 1946-1959 who have story of dipping snuff, 67 (44.6%) had ologically proven oral carcinomas, although es were available for only 48. All but 1 white, 35 were females and 12 males. Age ribution was: 1, age 39; 4, age 50-59; 15, 60-69; 23, age 70-79; and 5, age 80-84. sure of 13 pts. was 50-59 yr. and 8 from yr. In 19 pts. (40%), site of oral lesion esponded to the site where the snuff was . In 3 pts. who transferred the snuff from riginal site, a second lesion developed at ew location. The 48 pts. had a total of ancers: 29 invasive squamous carcinomas, ade 1 squamous carcinomas, and 13 verrucous inomas. Six pts. had leukoplakia.

259 MAST CELL REACTION AND 5-HYDROXYTRYPT- AMINE CONTENT IN THE SKIN OF SYRIAN EN HAMSTERS PAINTED WITH 9:10-DIMETHYL-1:2- ANTHRACENE. (E.) Chieco-Bianchi, L. (Inst. ol. Anat., U. Bari, Italy), L. Fiore-Donati, ennelli and G. Bertaccini. Nature (London) 293-294, 1963.

-Dimethyl-1,2-benzanthracene (DMBA; 0.1 ml, oln. in paraffin oil) was applied topically shaved area of the back of 20 Syrian golden ters (of both sexes), 2x/wk. for 7 wk.; 20 eated controls were sacrificed at the same . Bioassay of the 5-hydroxytryptamine (5-HT) ent of the skin and histological or UV ex- ation of mast cells revealed (a) there was a ed accumulation of mast cells in the painted s of the experimental animals; (b) these s were smaller and less granulated than al; (c) these cells did not fluoresce under ight, nor did the normal cells; (d) there

was no apparent elevation of the 5-HT skin level in either group. The lack of appreciable amounts of 5-HT in mast cells of DMBA-treated hamsters seems to indicate that this amine plays no significant part in the mast cell reaction de- veloping in the course of chemical skin carcino- genesis. (See also CRA 1(2):#230, 1963.)

63-1260 ELECTROPHORETIC SPECTRUM OF SERUM PROTEINS DURING MALIGNANT CHANGE INDUCED BY SEX HORMONES. (Rus.) Sidorik, E. P. (Kiev Res. Inst. Roentgen. Oncol., USSR). Vrach. Delo (7):83-86, 1963.

Ovariectomized rats (108) received monthly hex- estrol implants (3 mg s.c.) during the first months followed by 0.15 ml of a 0.1% soln. in an oil emulsion, for a total dose of 33-45 mg in 335-456 days. Prolonged admin. led to loss of body wt. and the formation of abscesses. Be- ginning in mo. 5 after treatment, some animals developed benign and malignant tumors of the external genitalia, mammary glands and the hypophysis. One rat developed a uterine adeno- carcinoma with metastases (no other details). In all animals undergoing malignant changes (no details) there was a decrease of serum albumin, γ - and β -globulins, albumin-globulin and albumin- γ -globulin ratios, and increases of α_1 and α_2 globulins. Total blood proteins decreased only in cases of generalized tumor processes.

63-1261 OBSERVATIONS ON HORMONAL CONTROL OF MAMMARY CANCER. I. ESTROGEN AND MAMMOTROPES. (E.) Kim, U. (Dept. Path., Francis Delafield Hosp., N.Y.), J. Furth and K. Yannopoulos. J. Nat. Cancer Inst. 31(2):233-259, 1963.

Groups of normal and hypophysectomized female W/Fu rats bearing 90-day-old transplants of the hor- mone responsive MT.W9A mammary adenocarcinoma were treated with estradiol-17 β (3 or 30 μ g 6x/wk. x 60 days) or with grafts of a mammotropin-secreting pituitary tumor MtT strain W5. Small doses of estradiol stimulated (+107 and +211%) and large doses of estradiol inhibited (-7 and -21%) the mammary tumor at 150 days in normal, but not in hypophysectomized rats. In contrast mammotropin tumor grafts stimulated mammary tumor grafts in hypophysectomized (+98 and +155%) and intact (+232 and +337%) rats. Increases in mammary tumor size were accompanied by increased plasma prolactin levels, whereas large doses of estradiol were accompanied by enlargement of pituitaries with increased prolactin content, but also by de- creased plasma prolactin levels. Plasma growth hormone levels were unchanged in estradiol-treated rats and increased in mammotropin-treated animals. It is concluded that small doses of estradiol specifically stimulate pituitary mammotropes, whereas large doses of estradiol prevent release of mammotropic hormone from the stimulated mammo- tropes, with possible consequent inhibition of hormone production.

- 63-1262 THE METABOLISM OF DIBENZ(a,h)ANTHRACENE. (E.) Van Duuren, B. L. (Inst. Indust. Med., New York U. Med. Ctr.). Acta Un. Int. Cancr. 19(3-4):524-527, 1963.

After exposure of rats to 1,2,5,6-dibenzanthracene (DBA) by aerosol (2 or 15 µg/DBA/l air for 1 hr.) or intratracheal inj. (2 mg/animal), rate of disappearance from the lung (from 1-24 hr.) was determined by spectroscopic procedures including fluorescence and UV spectroscopy. Among the metabolites identified in lung and skin tissue are 9,10-dibenzanthraquinone, 3,4-dibenzanthraquinone, 2-phenylphenanthrene-3,2'-dicarboxylic acid, 3-hydroxydibenzanthracene and 3,4-dihydro-3,4-dihydroxybenzanthracene. Several partially identified metabolites were obtained; these include phenols and phenol-quinones of DBA.

- 63-1263 CARCINOGENICITY OF OXY COMPOUNDS. (E.) Orris, L. (Inst. Indust. Med., New York U. Med. Ctr.), B. L. Van Duuren and N. Nelson. Acta Un. Int. Cancr. 19(3-4):644-647, 1963.

See CRA 1(6):#1090, 1963.

- 63-1264 CARCINOGENICITY AND CHEMICAL STRUCTURE OF NITROSAMINES. (E.) Druckrey, H. (Lab. Surg., Albert-Ludwigs-U., Freiburg, Germany), R. Preussmann and D. Schmähl. Acta Un. Int. Cancr. 19(3-4):510-512, 1963.

A brief discussion is presented of the relationships between chemical structure and carcinogenicity of about 40 different N,N-dialkyl nitrosamines and alkyl-acyl-nitrosamines studied mainly in BD rats after oral or parenteral admin. Carcinomas of the liver, esophagus, tongue, forestomach, bladder, kidneys and lungs were produced in practically all surviving animals, depending on structure, route of admin. and dosage of the respective compounds. The results strongly support the diazoalkane theory. In dialkyl nitrosamines the hydroxylation of an α -carbon atom is considered as the first step in metabolic activation. Nitrosamines are potent carcinogens, some with organ-specific effects and hence are useful in experimental carcinogenesis. (See also CRA 1(2):#217, 1963.)

- 63-1265 BLASTOMOGENIC PROPERTIES OF CERTAIN METABOLITES OF TRYPTOPHANE. (E.) Rauschenbach, M. O. (Centl. Inst. Hemat., Nivo Zikovskiy St. 4, Moscow), E. I. Jarova and T. G. Protasova. Acta Un. Int. Cancr. 19(3-4):660-662, 1963.

The leukemogenic activity of tryptophan metabolites was studied in 4-week-old C57 and CC57 mice by weekly inj. of 2.5 mg for 5-10 mo. or by daily addition to milk. Among 17/72 1-yr. survivors inj. with indol, 6/25 inj. with 5-hydroxyindolylacetic acid, and 19/57 inj. with

3-indolylacetic acid, there were 1 each adenocarcinoma of the breast. Myeloid leukemia developed in 1 out of 29/50 survivors given indolylacetic acid, 2 out of 19/57 given 3-indolylacetic acid and 6 out of 35/90 given 5-methyltryptophan. Leukemoid reaction was fairly frequent, including those given anthranilic acid and N/A-glucosyl/indol. The incidence of neoplasms in this series is below that reported by others.

- 63-1266 SELENIUM-CAUSED TUMOURS. (E.) Cherkes, L. A. (Inst. Nutr., Acad. Med. Sci. USSR, Moscow), M. N. Volgarev and S. G. Aptekar. Acta Un. Int. Cancr. 19(3-4):632-633, 1963.

See CRA 1(7):#1241, 1963.

- 63-1267 ESTIMATION OF CELL RENEWAL AND GROWTH IN RELATION TO MITOTIC COUNT AND MITOTIC DURATION IN EXPERIMENTAL SKIN CARCINOGENESIS. (E.) Evensen, A. (Inst. Gen. Exp. Path., U. Oslo, Norway). Acta Un. Int. Cancr. 19(3-4):582-583, 1963.

See CRA 1(6):#1050, 1963.

- 63-1268 CORRELATED CHEMICAL AND HISTOCHEMICAL STUDY OF EARLY ENZYMIC CHANGES IN RAT LIVERS DURING AZO DYE CARCINOGENESIS. (E.) Chang, J. P. (U. Texas M.D. Anderson Hosp., Houston), D. N. Ward and K. Ichinoe. Acta Un. Int. Cancr. 19(3-4):560-567, 1963.

Biochemical studies were carried out in the livers of young Sprague-Dawley rats 1, 2, 3, 5 and 7 days after start of feeding with 3'-methyl-4'-dimethylaminoazobenzene (0.06%). (1) The glycogen metabolism was altered in the same manner in fasted and dye-fed rats at the beginning of the experiments, although glycogen was restored to normal level after 7 days of dye feeding. (2) Of the enzymes studied in azo dye-fed rats, alkaline and acid phosphatase, ATPase, glucose-6-phosphatase and DPNH diaphorase showed little change; 5'-nucleotidase showed a decrease while TPNH diaphorase was increased. (3) ATPase staining in bile canaliculi was markedly decreased in livers of dye-fed rats, while it was intensified in the bile canaliculi of fasted rat livers toward the end of the experiment. (4) The behavior of chemical substances in fasted rat livers differed from that in livers of dye-fed animals. (5) Some histochemical and chemical data agreed remarkably well, while certain histochemical changes could not be detected by chemical assay.

- 63-1269 THE ROLE OF COMBINED EFFECT OF LOCAL AND GENERAL ETIOLOGICAL FACTORS IN THE INDUCTION OF CARCINOMA OF THE UTERINE CERVIX, VAGINA AND URETHRA IN MICE. (E.) Young Gang (Dept. Path. Anat., Chinese Acad. Med. Sci., Peking), Gou Zen and Chen Mou Line. Acta Un. Int. Cancr. 19(3-4):674-677, 1963.

a study of multiple factors in the etiology of carcinoma of the cervix in strain A and "mating" mice, 5 factors were used: human carcinoma (S), chronic cervical trauma (T), a supernatant fluid of human cancer tissue (C), hormonal imbalance (H) produced by inj. of estradiol and testosterone and over-stimulation of the higher nervous system (N). Mice were sacrificed at different intervals and examined histologically. The experiment was carried out in 4 groups. Invasive carcinoma of the cervix, vagina and urethra was induced earlier and in greater numbers under the combined effect of multiple local and general factors (HTCS, NHTCS, HTS, S, NH-NHTS, H-HTS, etc.). It was also induced under the simpler combination of factors (TS, S and H-TH), provided the time of the experiment was sufficiently prolonged. No carcinoma was induced in the groups in which a single factor (T or H) was used. It is considered that the local factor S and the general factor H are 2 carcinogens and that the local factor T is a cocarcinogen.

1270 THE EFFECTS OF BENZO(a)PYRENE, CIGARETTE SMOKE CONDENSATE AND ATMOSPHERIC POLLUTANTS ON THE RESPIRATORY SYSTEM OF SYRIAN HAMSTERS. (E.) Herrold, K. McD. (NCI, Bethesda). *Acta Un. Int. Cancr.* 19(3-4):710-714, 1963.

Sign and malignant tumors of the trachea, bronchi, and bronchioles have been induced in Syrian hamsters following the intratracheal instillation of 3,4-benzpyrene (BP) suspended in olive oil. So far only atypical epithelial changes, suggestive of precancerous lesions, have been observed with BP suspended in distilled water. Significant changes were noted in the animals that received intratracheal BP in olive oil. The findings suggest that both the vehicle and the physical state of the carcinogen are important factors in carcinogenesis. The intratracheal instillation of cigarette smoke condensate and atmospheric pollutants produced regenerative epithelial changes of the tracheobronchial mucosa. These lesions included basal cell hyperplasia, and peribronchial and peribronchiolar proliferation. Atmospheric pollutants often induced extensive adenomatous proliferation that involved large areas of the lung. No tumors of the respiratory tract have been induced with cigarette smoke condensate or atmospheric pollutants.

1271 INDUCTION OF LUNG CANCER IN RATS BY INTRATRACHEAL INSUFFLATION OF CARCINOGENIC HYDROCARBONS. (E.) Pylev, L. N. (Inst. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). *Acta Un. Int. Cancr.* 19(3-4):688-691, 1963.

Carcinogens suspended in a protein colloidal solution, with some India ink added to aid in visualization, were placed by intubation into the trachea of Wistar and random bred rats. In 3

groups, 9,10-dimethyl-1,2-benzanthracene (DMBA) was given in a single dose of 2.5 mg, and in 3 or 5 monthly doses of 2 mg each. Two groups of rats were given 3,4-benzpyrene (BP), 5 or 7 monthly doses of 5 mg each. First tumors appeared in 5 mo. In 216 rats given DMBA, 40 developed squamous and 2 adenocarcinomas of the lung (27.5%); most appeared in those that received 3 or 5 doses. At the time of writing, 19/54 BP animals have died and 12 of these showed squamous carcinoma. It is possible that the India ink not only facilitated localization but may have hindered excretion of the carcinogen from the lung.

63-1272 THE MECHANISM OF CARCINOGENESIS IN BREAST TUMOUR DEVELOPMENT IN MICE. (E.) Haran-Ghera, N. (Dept. Exp. Biol., Weizmann Inst. Sci., Rehovoth, Israel). *Acta Un. Int. Cancr.* 19(3-4):765-768, 1963.

Using LAF₁ mice, in which mammary tumors do not occur spontaneously, 20-methylcholanthrene (20-Me; 0.25% in acetone, applied to skin one or six times at 2 wk. intervals) failed to induce such tumors, whereas urethan (U; 20 mg x 1/wk. x 10 i.p.) was slightly carcinogenic. Mammary tumors were, however, readily produced in such mice by prolonged hormonal imbalance, following the transplantation of a single hypophysis beneath the kidney capsule. A cocarcinogenic action was demonstrated when the hormonal stimulation was made to act concurrently with U or with 20-Me, though a two-stage mechanism did not seem to be involved. Different morphological types of mammary tumors were observed: mice treated with the hypophyseal graft only, or with the hypophyseal graft followed by a carcinogen, developed only adenocarcinomas with acinar formation, whereas the concurrent action of both treatments induced many tumors of the adenocanthoma and carcinosarcoma types.

63-1273 QUANTITATIVE CYTOCHEMISTRY OF THE CARCINOGENESIS IN THE RAT LIVER. (E.) Grundmann, E. (Inst. Path., Albert-Ludwigs-U., Freiburg, Germany). *Acta Un. Int. Cancr.* 19(3-4):571-575, 1963.

Using cytological and cytophotometric methods changes were investigated in rat liver during carcinogenesis by means of diethylnitrosamine. Initially there is an increase in cytoplasmic RNA in the periphery of the liver lobule. At the same time the nuclei increase in size and in DNA content; many of them become polyploid. The cells swell and lose their protein in the cytoplasm. When carcinoma begins in the centrolobular zones small basophilic cells quickly appear, which have a cytoplasmic RNA content up to 3x the normal value. In these cells cytoplasmic RNA is no longer clumped but is diffuse or lamellar, and nuclear DNA is exactly diploid in amount. These primary nests of malignant cells enlarge into typical carcinoma nodules. In these the cytoplasmic RNA is mostly increased and nuclear DNA

values reflect aneuploidy, scattered about a stem line value.

- 63-1274 THE EFFECT OF PHYSICAL FORM OF IMPLANT ON NICKEL SULPHIDE TUMOURIGENESIS IN THE RAT. (E.) Gilman, J. P. W. (Div. Microscop. Anat., Ontario Vet. Coll., Guelph, Canada) and H. Herchen. *Acta Un. Int. Cancr.* 19(3-4):615-619, 1963.

Groups of rats were exposed to single i.m. implantations of nickel sulfide (Ni_3S_2) as free powder, powder contained in diffusion chambers, chips and discs. These differences in physical form had no significant effect on tumor incidence, which ranged from 71 to 95%. However, the av. latent period was almost doubled when the carcinogen was contained in diffusion chambers. Tumors were all locally occurring rhabdomyosarcomas and exhibited a high incidence of metastases. It was shown that neither the walling off of the metal implants nor phagocytosis nor direct contact between metal particles and cell are necessary to the mechanism of tumorigenesis with nickel or cobalt compounds.

- 63-1275 ON THE PRESENCE OF ENDOGENOUS LEUKEMOGENOUS FACTORS IN THE URINE OF LEUKAEMIA CASES. (E.) Derviz, G. V. (Centl. Inst. Hemat. Blood Transf. (Order Lenin), Moscow), N. M. Nemenova and R. E. Kimeral. *Acta Un. Int. Cancr.* 19(3-4):663-664, 1963.

Leukemogenic action of two fractions of the urine of leukemic pts. was studied. a) The urine was extracted with butyl alcohol (BA) and the urine factors were concentrated 400-500 fold. b) Other portions of the urine were dialyzed against tap water and the soln. of macromolecular non-dialyzable material obtained in this way was lyophilized. Low leukemia mice C57Bl and CC57Br were given six s.c. inj. at monthly intervals, of 0.3 ml (0.1 gm of the lyophilized substance) or a single inj. into the spleen of 0.1-0.05 ml. Leukemogenic effects were seen in the organs of mice treated with the BA extract. Multiple s.c. inj. of this fraction produced leukemia in 33 of the animals with an av. incubation period of 15 mo. With inj. into the spleen the frequency was lower (17%), but latency shorter (7 mo.). The extracts of normal urine inj. into the spleen produced leukemia in only 4% of the cases.

- 63-1276 EXPERIMENTAL PRODUCTION OF A BIOLOGICAL MODEL OF RAT BRAIN TUMOUR INDUCED WITH 9,10-DIMETHYL-1,2-BENZANTHRACENE/DMBA. (E.) Dimant, I. N. (Sci. Res. Inst. Roentgenol., Radiol. Oncol. Min. Health Uzbek, SSR) and D. M. Abdurasulov. *Acta Un. Int. Cancr.* 19(3-4):774-775, 1963.

Cerebral tumors were induced by the intracerebral implantation of pellets of 9,10-dimethyl-1,2-

benzanthracene (3 mg, alone or with casein) in approx. 90% of 70 albino rats of both sexes after they had been subjected to hormonal imbalance by prior hypophysectomy, pinealectomy, adrenalectomy, thyroidectomy or gonadectomy. Carcinogen was implanted 1.5 mo. after the operative procedures. Average latent period was within 2-5 mo. In the control group no tumors developed within 8 mo. The cerebral neoplasms involved extensive zones of the hemisphere. They presented complex histological structure and were composed of neuroectodermal and mesenchymal elements regenerated to blastomas. The nature and degree of malignancy depended, to a certain extent, on the kind of experimentally produced hormonal disruption. Increase in incidence of tumors (up to 100%) and the malignant change of some of them were observed by transplantations. Immunological studies indicate the induced tumors are true cerebral neoplasms.

- 63-1277 IMMUNOLOGICAL STUDIES OF RAT LIVER CELL ANTIGENS DURING AZO DYE CARCINOGENESIS. (E.) Baldwin, R. W. (Cancer Res. Dept., U. Nottingham, England). *Acta Un. Int. Cancr.* 19(3-4):545-548, 1963.

The antigenic composition of subcellular fraction of liver were investigated in rats undergoing carcinogenesis by feeding them dimethylaminoazobenzene in a low protein diet. Several normal liver cell sap antigens were found to be deleted from liver tumor. In addition, two major antigenic components detectable in deoxycholate solubilized preparations of normal liver microsomes were absent from tumor. The antigenic composition of subcellular fractions prepared from apparently normal liver taken from tumor-bearing rats did not differ from those of normal liver fractions. It was concluded, therefore, that the deletion of cell antigens occurred during tumor induction and not as a result of nonspecific dietary effects during carcinogenesis treatment.

- 63-1278 ON MALIGNIZATION OF RAT FIBROBLASTS IN TISSUE CULTURE. (E.) Benevolenskaya, S. V. (Berogvaia 11, District 39, Moscow) and N. S. Staroverova. *Acta Un. Int. Cancr.* 19(3-4):624-628, 1963.

Earlier studies demonstrated that malignant change of rat fibroblasts in tissue cultures required 6-8 mo. and only with the combined action of 20-methylcholanthrene and extracts from certain malignant human and rat tumors. More recent studies have shown that malignant change inevitably occurred at 6-8 mo. of cultivation of rat fibroblasts as monolayer cultures, irrespective of all other influences. This was proved by biological testing. It was shown that by the time malignant change occurred the majority of cells had transformed from diploid to hypotetraploid, and that the karyologic changes had appeared before it was possible to demonstrate malignant change by biological testing.

63-1279 THE CARCINOGENICITY AND REACTIVITY TO TISSUE CONSTITUENTS OF 4-NITROQUINOLINE-N-OXIDE. (E.) Searle, C. E. (Dept. Path., Med. School, Birmingham, England) and D. L. Woodhouse. *Acta Un. Int. Cancr.* 19(3-4):519-521, 1963.

The carcinogenicity of 4-nitroquinoline-N-oxide (NQO) for mouse skin has been confirmed, and skin tumors have also been induced in hamsters but not in guinea pigs. NQO reacted with a range of SH-containing compounds with release of nitrite, but not with various disulfides, thioethers, urea derivatives or sulfur-free compounds. Interaction of NQO with various tissues gave results for SH-content agreeing with those reported by other workers using different techniques. Application to mouse skin of 0.2% benzpyrene and 0.3% NQO in acetone alternately resulted in fewer tumors than were obtained by similar treatment with benzpyrene only.

63-1280 MELANOMAS OF THE SKIN OF GUINEA PIGS FOLLOWING THE APPLICATION OF A SOLUTION OF 9,10-DIMETHYL-1,2-BENZANTHRACENE IN BENZENE. (E.) Edgcomb, J. H. (NCI, Bethesda) and H. Mitchelich. *Acta Un. Int. Cancr.* 19(3-4):707, 1963.

9,10-Dimethyl-1,2-benzanthracene (DMBA; 0.1 ml of a 0.5% soln. in benzene) was applied weekly to the dorsal skins of 52 guinea pigs, starting at age 2-3 mo. Epilated areas, cutaneous horns, nodoid and epidermoid cysts, small papillomas, pigmented nevi resembling junctional nevi developed at or near the site of application in all animals. Four animals developed malignant melanomas at the site of application when they were 2-4 yr. of age. Attempts to transplant the tumors to X-irradiated, newborn, and cortisonized guinea pigs have been unsuccessful. Histopathological observations suggest that the melanomas arise from junctional nevi which appear in the skin after the initial application of DMBA.

63-1281 THE METABOLISM OF N-2-FLUORENYLACETAMIDE IN THE RHESUS MONKEY. (E.) Dyer, H. M. (NCI, Bethesda) and M. G. Kelly. *Acta Un. Int. Cancr.* 19(3-4):502-506, 1963.

A group of 4 young rhesus monkeys were used for 2-5 times, at intervals over a 10-month period. They were fed N-2-fluorenylacetylamide (2-FAA) 5-7 x/wk. in doses increasing gradually from 6 to 60 mg. To date no evidence of tumor induction has appeared to suggest cause for concern. Metabolism experiments have shown that these monkeys resemble the guinea pig more than the rat in the rate of excretion and in the large amounts of the 7-hydroxy metabolite excreted in urine. However, in the production of N-OH-2-FAA and in tolerance of 2-FAA the monkey may be more like the rat than the guinea pig. Thus, if the N-hydroxy metabolite of 2-FAA is involved in the carcinogenic process, as has been suggested

for rats, it may be that with sufficient time cancer will be induced in the monkey by feeding 2-FAA.

63-1282 COMBINED EFFECTS OF METHYLCHOLANTHRENE AND VACCINIA VIRUS IN CORTISONE-TREATED AND UNTREATED MICE. (E.) Duran-Reynals, M. L. (Yale U. Sch. Med., New Haven, Conn.). *Acta Un. Int. Cancr.* 19(3-4):792-796, 1963.

Mice rendered susceptible to vaccinia dermal infection by cortisone inj. and untreated mice received 20-methylcholanthrene (MC) skin paintings at the site of virus infection. Under certain conditions, the MC applied before virus inoc. inhibited the virus-induced skin ulcers; applied after it enhanced them. Mice with the more severe ulcers developed the highest incidence of benign or malignant skin tumors and/or lymphomas with the smallest amount of MC used. These and other published findings suggest that the possibility of developing neoplasia is increased in a host exposed to chemical carcinogens during acute viral infection.

63-1283 COMPARISON OF THE UPTAKE AND RETENTION OF CARCINOGEN BY BREAST AND FAT (AFTER FEEDING) AND SKIN (AFTER TOPICAL APPLICATION). (E.) Bock, F. G. (Roswell Park Mem. Inst., Springville, N.Y.). *Acta Un. Int. Cancr.* 19(3-4):789-791, 1963.

Localization of hydrocarbon in the breast depends upon the conc. of the compound in the mammary fat pad and is thus affected by the species and strain used. Studies of the localization of 3,4-benzpyrene in the skin (after topical application) and fat (after oral feeding) in A/St and JK/St mice suggest that some species and strain differences are due to the volume of the adipose tissue receiving the carcinogen. In fat animals, the hydrocarbon is diluted in a large volume of adipose tissue. To the extent that genetic factors affect the total amount of adipose tissue, they also affect the localization of hydrocarbon in the fat and breast. Following skin painting, hydrocarbons move directly to the target area. Although the specific mechanisms of genetic influence are obscure, preliminary experiments suggest that three or more genetic factors affect this process, with factors that retard penetration exhibiting dominance. (See also CRA 1(3):#396, 1963.)

63-1284 SUBCUTANEOUS NEOPLASMS INDUCED BY TRYPAN BLUE. (E.) Brown, D. V. (VA Hosp., Seattle, Wash.). *Acta Un. Int. Cancr.* 19(3-4):655-656, 1963.

Trypan blue, at an optimal dose of 10 mg/100 g, s.c. every 2 wk., produced s.c. tumors in 45% of the rats treated, with a latent period of 11-17 mo. Although uniform in their growth pattern and

gross appearance, the neoplasms showed a variable histologic pattern which, in some of the tumors, suggested a histogenic relationship to the neoplasms of the reticuloendothelial system. The development of both types of tumors in the same animal supported this concept. The tumors of the liver have been successfully transplanted.

63-1285 CARCINOGENIC ACTIVITY OF ANALOGUES OF p-DIMETHYLAMINOAZOBENZENE. (E.)

Brown, E. V. (U. Kentucky, Lexington). Acta Un. Int. Cancr. 19(3-4):531-533, 1963.

It has been shown that there is a wide range of activity in the six possible isomers of the mono-pyridine and pyridine-N-oxide analogs of p-dimethylaminoazobenzene (DAB; butter yellow). Subsequently it has been shown that the seven isomers of N,N-dimethyl-p-quinolylazoaniline and their seven N-oxides show an even greater range of activity. This report discusses the hepatocarcinogenic activity of the isomeric N,N-dimethyl-p-isoquinolylazoanilines and the activity of the following analogs of DAB: tetrahydronaphthalene, 2-anthracene, 1-2-anthraquinone, 2-benzothiazole, 3-diphenylthiophene, 2-dibenzofuran, 6-quinoxaline. Rough quantitative values are given for their relative tumor producing activity.

63-1286 INFLUENCE OF A DIET LOW IN PYRIDOXINE ON TUMORIGENESIS IN RATS INGESTING N-2-FLUORENYLACETAMIDE. (E.)

Morris, H. P. (NCI, Bethesda), H. Sidransky and B. P. Wagner. Tumori 49(3):159-171, 1963.

Early histological changes in the liver and cancer development in the liver and at other sites have been studied in male and female Buffalo strain rats ingesting a diet containing N-2-fluorenylacetamide (2-FAA; 0.03%) and a low level of pyridoxine-HCl (0.25 µg/g of diet). A month's delay in the appearance in the liver of mitotic figures in bile duct cells and in the gradual increase in number of oval or ductal cells in the periportal areas were found in the low-pyridoxine groups when compared to previous studies with diets containing 2-FAA and high in pyridoxine. The overall incidence of liver tumors induced by 2-FAA was not influenced by a low level of dietary pyridoxine, but there was a delayed appearance of tumors. Males fed the low pyridoxine-2-FAA diet developed a higher incidence of liver tumors than did females. The highest incidence of ear duct tumors developed in females. These females had the longest survival. The amount of 2-FAA ingested does not appear to have been a deciding factor in the development of tumors in this experiment.

63-1287 BINDING OF FLUORENYLACETAMIDE TO RAT LIVER RIBONUCLEIC ACID (RNA) IN VIVO. (E.)

Henshaw, E. C. (Harvard Sch. Med., Boston, Mass.) and H. H. Hiatt. Proc. Am. Assn. Cancer Res. 4(1):27, 1963.

Sucrose density gradient analysis of phenol-purified nuclear RNA prepared from rat liver 4 after i.p. inj. of radioactive N-2-fluorenylacetamide (FAA) revealed uniform labeling of the 28 S and 18 S (ribosomal) RNA. There was no evidence to suggest preferential binding to the heterogeneous RNA which is labeled early by radioactive RNA precursors, and which may include messenger RNA. The pattern of labeling suggested attachment to pre-formed RNA, rather than incorporation during synthesis. Cytoplasmic and nuclear ribosomal RNA's were labeled to a similar extent. However, cytoplasmic 4 S (soluble) RNA was preferentially labeled, with specific activity 3x that of ribosomal RNA. Specific activities of nuclear and cytoplasmic RNA were still equal to each other 72 hr. after FAA inj., thus giving no suggestion of flow of label from one compartment to the other during this period. Binding to DNA, if any, was too slight to be clearly demonstrable.

63-1288 PREVENTIVE EFFECT OF NORANDROSTENOLONE PHENYLPROPIONATE ON EXPERIMENTAL TUMOR FORMATION. (Fr.)

Verne, J. (Histol. Lab., Fac. Med. Paris) and P. C.-J. Roth. Bull. Assn. Franc. Cancer 50(1):49-52, 1963.

The carcinogenic effect following the s.c. implantation of dihydrofolliculine (2-10 mg) in female RIII and C3H mice was largely prevented when followed 8 days later by inj. of norandrosthenolone phenylpropionate (24 µg/wk. x 10, then 48 µg/wk. up to x 6). After treatment with dihydrofolliculine only, 2/9 RIII and 4/4 C3H mice developed cancers compared with cancers in only 0/76 and 9/26, resp., in mice which had also received norandrosthenolone phenylpropionate.

63-1289 STUDIES ON LEUKEMOGENESIS IN URETHAN-TREATED MICE. (E.)

Della Porta, G. (Natl. Inst. Study Cure Cancer, Milan, Italy), J. Capitano and P. S. De Castillia. Acta Un. Int. Cancr. 19(3-4):783-785, 1963.

Urethan given to 5-week-old outbred albino mice (0.4% in the drinking water either for 20 or for 10 days) was lethal to many. Among the animals surviving at the 15th wk. of age, malignant lymphomas developed in 32.8% of 70 females and 37.5% of 40 males in the group treated for 20 days, and 16.8% of 83 and 31.1% of 61, resp., in the group treated for 10 days only. Most of the malignant lymphomas were thymic lymphosarcomas and arose before the 40th wk. of age. In the controls there were 0.9% lymphomas among 120 females and 3.8% among 130 males. Among other tumors which occurred in the treated animals, lung adenomas reached 80% incidence and mammary tumors developed in 35.9% of the females. In control virgin females there were 12.6% mammary tumors, with an av. latent period 10 wk. longer than in the treated animals.

1290 INFLUENCE OF AGE AND ROUTE OF ADMINISTRATION ON LUNG CARCINOGENESIS BY THAN IN SWISS MICE. (E.) De Benedictis, G. (Inst. Anat. Path., U. Bari, Italy), L. Chieco-Bianchi, G. Maiorano and L. Fiore-Donati. Acta Int. Cancr. 19(3-4):695-696, 1963.

CRA 1(3):#413, 1963.

1291 THE INDUCTION OF TUMORS IN MONKEYS AND RABBITS BY CHEMICAL AND RADIATION. (E.) Mel'nikov, R. A. (Inst. Oncol., J. Med. Sci. USSR, Leningrad). Acta Un. Int. Cancr. 19(3-4):708-709, 1963.

Animals containing isotopes were introduced into the front wall of the upper jaw of rhesus monkeys. Three received Ag^{110} (0.82-1.109 mC) and Co^{60} (0.57 mC). Two of each group developed malignant tumors within 569-1044 days: fusiform, polymorphocellular and fibrosarcoma of the upper jaw, and squamous-cell, horny cancer of the mucous membrane of the maxillary sinus. In addition, one monkey developed a squamous cornifying cancer of the tongue. Additional experiments were conducted in 68 rabbits with chemical carcinogens (methylcholanthrene 15-20 mg, 9,10-dimethyl-1,2-benzanthracene 8-12 mg). Specific, pretumor and completely formed oral lesions were observed. Study of the induced malignant tumors of the upper jaw and maxillary sinus in monkeys reveals similarity, from the clinical point of view, to the course of the illness in man and may be used as an experimental model.

1292 THE EFFECT OF ADRENALECTOMY AND OF DESOXYCORTICOSTERONE ACETATE DURING EARLY AND LATE STAGES OF LIVER CARCINOGENESIS IN RATS FED p-DIMETHYLAMINOAZOBENZENE. (E.) Konidis, A. (Dept. Path., Aristotelian U. of Thessaloniki, Greece). Acta Un. Int. Cancr. 19(3-4):771-773, 1963.

Adrenalectomy and desoxycorticosterone acetate treatment in rats fed dimethylaminoazobenzene reduces its inhibitory effect on liver tumor formation during the early stages of carcinogenesis. After the tumor anlage is established in the liver, this treatment has no effect.

1293 AMINOAZO DYE AMINO-OXIDE AS A POSSIBLE INTERMEDIATE METABOLITE PRECEDING TO DIMETHYLAMINOAZOBENZENE. (E.) Terayama, H. (Inst. Biophys. Biochem., U. Tokyo). Acta Un. Int. Cancr. 19(3-4):534-538, 1963.

Test the idea that dimethylaminoazobenzene amino-oxide (DAB-N-oxide) may be an intermediate metabolite preceding N-demethylation of dimethylaminoazobenzene (DAB), reactions of DAB-N-oxide synthesized from DAB and perbenzoic acid were

studied. It was found that when DAB-N-oxide was incubated with iron-porphyrin compounds such as hemin, hematin, hemoglobin and methemoglobin, rapid decomposition of the N-oxide took place, generating large amounts of demethylated aminoazo dye (MAB), DAB, 3-HO-DAB as well as lesser amounts of amino benzene and 3-HO-MAB. When proteins or amino acids were also present in the reaction mixture, considerable quantities of protein- or amino-acid-bound aminoazo dyes were formed. A polar dye similar to that obtained from liver proteins of rats fed with DAB was obtained from the hydrolysate of proteins incubated together with DAB-N-oxide and hematin.

63-1294 ENDOGENOUS AND EXOGENOUS FACTORS IN CHEMICAL CARCINOGENESIS BY N-2-FLUORENYL-ACETAMIDE. (E.) Weisburger, J. H. (NCI, Bethesda) and E. K. Weisburger. Acta Un. Int. Cancr. 19(3-4):513-518, 1963.

ACI strain rats were given C^{14} -N-2-fluorenyl-acetamide i.p. The urinary metabolites and the amount of isotope bound to liver constituents were similar in male and female immature rats. However, mature animals exhibited quantitative differences. Males had higher radioactivity in feces and liver proteins; females in the urine and the glucosiduronic acid fraction of the urine. Hypophysectomized male rats excreted slightly less of a dose in urine and feces than pair-fed controls. However, the liver proteins exhibited similar isotope content in both groups. Male rats pretreated 48 hr. earlier with CCl_4 also had analogous specific activities in liver proteins as compared to their controls. A model is described visualizing the development of tumors as a result of the concerted action of the exogenous chemical carcinogen and of endogenous factors stimulated or elicited by the chemical.

63-1295 EFFECT OF 3-METHYLCHOLANTHRENE ON AMINO ACID INCORPORATION INTO RAT LIVER PROTEIN. (E.) Gelboin, H. V. (Natl. Inst. Ment. Health, Bethesda, Md.) and L. Sokoloff. Acta Un. Int. Cancr. 19(3-4):568-570, 1963.

In vivo admin. of 20-methylcholanthrene (MC) into rats rapidly alters the amino acid incorporating activity of a system of liver mitochondria, microsomes, and supernatant fluid. Thus 1 hr. after the i.p. inj. of MC the in vitro incorporation of DL-leucine- C^{14} into liver proteins increases by 20%; at 18 hr. the increase is average 70%. Each subcellular component of the system contributes to the overall MC effect. Thus, with microsomes from either normal or MC-treated rats there is a greater incorporation with MC supernatant fluid added than with equivalent amounts of normal supernatant. The stimulatory effect is not affected by heating at 100°C. Differences between the normal and MC supernatant fractions can be eliminated by the addition of saturating levels of GTP.

Greater capacity for incorporating amino acids of MC microsomes is not due to a variation in the known cofactor levels of the system. At least part of the stimulatory effect in the microsomes has been localized to the step in which soluble RNA bound amino acids are incorporated into microsomal protein. (See also CRA 1(5):#877, 1963.)

63-1296 ACTIVITY OF FRACTIONS OF TOBACCO SMOKE CONDENSATE IN THE SEBACEOUS GLAND SUPPRESSION TEST. (E.) Kracht, J. (Inst. Path., U. Hamburg Chem. Inst., Germany), G. Grimmer and E. Hübner. Acta Un. Int. Cancr. 19(3-4):724-729, 1963.

Four main fractions of tobacco smoke condensates have been examined by the sebaceous gland suppression test. (1) The polycyclic hydrocarbons display the most intense activity which quantitatively corresponds to that of the original condensate. (2) The acidic and phenolic fractions provoke gland suppression only when relatively high doses are applied. (3) The activity of neutral fractions is rather insignificant. (4) The basic fraction does not cause suppression at all. The recombined fractions are almost as active as the original condensate. Four subfractions of the aromatic hydrocarbons (not yet chemically defined) were eluted by solvents of increasing polarity. None of these subfractions has an activity corresponding to that of the total fraction of the aromatic hydrocarbons, however, the sum of the activities is equivalent to that of the total fraction.

63-1297 INDUCTION OF PULMONARY ADENOMATOSIS IN DBA/2 MICE BY THE ORAL ADMINISTRATION OF DIBENZ(a,h)ANTHRACENE. (E.) Snell, K. C. (NCI, Bethesda) and H. L. Stewart. Acta Un. Int. Cancr. 19(3-4):692-694, 1963.

An olive oil emulsion of 1,2,5,6-dibenzanthracene was added to the drinking water of DBA/2 mice for 200 days; av. daily intake for 14 males and 13 females was 0.8 and 0.76 mg, resp. All animals developed pulmonary adenomatosis. The lesion was found also in one control mouse given only olive oil. Mice that drank the emulsion containing dibenzanthracene developed alveolar carcinoma, tumors of the mammary gland, precancerous lesions of the small intestine, and hemangioendotheliomas involving the pancreas, mesentery, and abdominal lymph nodes.

63-1298 ON SUBSTANCES INDUCING CANCER OF THE BLADDER. (E.) Walpole, A. L. (Imperial Chem. Indust. Ltd., Alderley Park, Macclesfield, Cheshire, England). Acta Un. Int. Cancr. 19(3-4):483, 1963.

Auramine, fed at 0.1% in the diet to 12 male rats for 87 wk. resulted in 11 with hepatomas. Another

group was given auramine in oil (2.5% suspension, 0.1 ml/100 g, s.c. 5x/wk. x 21); among 20 survivors after 40 wk., 3 developed hepatomas, 3 intestinal carcinomas, and 11 s.c. sarcomas at the site of inj. In mice given auramine at 0.1% in the diet for 1 yr., 4/7 males and 3/10 females dying after 50 wk. or more had developed hepatomas. In CBA mice given auramine at 0.2% in the diet for a yr., incidence of hepatomas in 12 males and 15 females surviving at 50 wk. rose to 58% and 53%, resp.; in controls, incidence was 11% and 3%, resp. No abnormalities have been noted in chronic experiments in dogs which have now received an av. of 66 g of the dyestuff.

63-1299 STUDIES ON CHEMICALLY INDUCED BREAST TUMOURS IN THE RAT. (E.) Howell, J. S. (Dept. Path., Sch. Med., Birmingham, England). Acta Un. Int. Cancr. 19(3-4):762-764, 1963.

9,10-Dimethyl-1,2-benzanthracene (DMBA; 1.6% in oil) was applied to the skin of female rats (Birmingham strain) at intervals of 2 wk.; each application averaged 20.8 mg. Ovariectomy or adrenalectomy 2 wk. after 6 applications of DMBA reduced the number of induced breast tumors. Puromycin aminonucleoside (i.v.), which produces proteinuria, also reduced the incidence of breast tumors.

63-1300 LOCAL INHIBITION AND ENHANCEMENT OF GROWTH OF TRANSPLANTED TUMOR CELLS IN MICE. (E.) Gitlitz, G. F. (Surg. Div., Montefiore Hosp., New York), A. G. Ship, J. L. Glick and A. H. Glick. J. Surg. Res. 3(8):370-376, 1963.

Treatment of white mice with formaldehyde (0.05% soln., 5 ml), 1, 24 or 48 hr. before implantation of Krebs 2 carcinoma in air bubble wounds, enhanced tumor growth and shortened the latent period by 33-50%. The combination of pre- and post-treatment with formaldehyde was significantly less effective in inhibiting tumor growth than the post treatment alone. Treatment with formic acid (0.4% soln., 2 ml) appeared to enhance tumor growth, but due to the invasive growth, this could not be substantiated by objective measurements; there was no effect on the latent period.

63-1301 ACQUIRED CHROMOSOMAL ANOMALIES INDUCED IN MICE BY INJECTION OF A TERATOGEN IN PREGNANCY. (E.) Ingalls, T. H. (Henry Phipps Inst., U. Pennsylvania Sch. Med., Philadelphia), E. F. Ingenito and F. J. Curley. Science 141: 810-812, 1963.

When 6-aminonicotinamide was admin. to pregnant mice on approx. the 13th day of gestation, 95% of the embryos subsequently manifested cleft palates. Explanted embryonic tissue showed chromosomal anomalies not only in cells adjacent to palatal defects but also in muscle, skin and limb fragments

204 embryonic metaphase cells counted 1 day after maternal inj. and 395 counted 6 days after inj., a normal pattern was seen in 41.7% and 33%, resp., controls, 94.5%; polyploidy was seen in 47.5% and 9.1%, resp., controls, 1.8%; and fragmentation in 10.8% and 29.6%, resp., controls, 3.6%. Of 84 maternal bone marrow cells studied microscopically, a normal pattern was seen in 35.7%, controls, 86.2%; polyploidy, 10%, controls, 3.8%; and fragmentation 58.3%, controls, 10.1%.

1302 ON THE BLASTOMOGENIC ACTION OF THE ESTONIAN SHALE OIL SOOT AND THE SOOT OF LIQUID FUEL OBTAINED FROM THE PROCESSING OF SHALE OIL. (E.) Vosamae, A. (Narvskoe St., K. K. K. 24, Tallin, USSR). *Acta Un. Int. Cancr.* 19(3-4):739-741, 1963.

In chronic experiments, benzene extracts from Estonian shale oil (solid fuel) soot and the soot of liquid fuel (mazut) were painted on the skins of white mice. Experiments showed that the benzene extract of shale oil (solid fuel) soot, containing 3,4-benzpyrene (determined by fluorescent spectroscopy) proved to be strongly carcinogenic. This extract produced benign and malignant tumors in most of the animals. The results of the second series of experiments demonstrated that the benzene extract of mazut soot exerts considerably less carcinogenic action than the extract of soot of solid shale oil.

1303 CHANGES OF THE SUB-EPITHELIAL CONNECTIVE TISSUES IN THE EARLY STAGES OF SKIN CARCINOGENESIS INDUCED BY CHEMICAL AGENTS. (E.) Toni, C. (Gen. Inst. Path., U. Bologna, Italy) and F. Zajdela. *Acta Un. Int. Cancr.* 19(3-4):555-559, 1963.

Changes in the sub-epithelial connective tissue during early stages of carcinogenesis were studied after topical treatment of mice with 9,10-dimethyl-1,2-benzanthracene (DMBA); rabbits with 1,2,3,4-dimethylcholanthrene (20-Me), 10-methyl-1,2-benzacridine, 3,4-benzpyrene, and croton oil; and rats and guinea pigs with DMBA. Whatever the animal species and the carcinogenic compound used, the changes of the subepithelial connective tissues are similar: they consist of the gradual replacement of the fibrous dermis and of the basal membrane by an immature, loose connective tissue, which does not undergo fibrosis. The sequence of these changes parallels the responsiveness of the animals to skin carcinogenesis and the carcinogenic potency of the compounds.

1304 EFFECTS OF SEX HORMONES ON THE EXCRETION OF BLASTOMOGENIC AZO-DYE IN URINE. (E.) Belitsky, G. A. (Inst. Exp. Clin. Med., Acad. Med. Sci., Moscow). *Acta Un. Int. Cancr.* 19(3-4):769-770, 1963.

Influence of sex hormones upon the excretion

of o-aminoazotoluene (OAAT) (in the form of pellet implants) in urine was studied in CC57br and 020 mice. In intact males and castrates of both sexes, which received testosterone, OAAT was excreted in both the free and protein-bound form. The intact females, castrates of both sexes, which received no hormones, as well as ovariectomized females treated with estrogen, excreted no protein in urine. These animals excreted only free OAAT and the conc. of dye in their urine was much higher than in the first group of animals. The low incidence of hepatomas in animals which receive androgen may be correlated with their ability to excrete the carcinogen in both the free and protein-bound form.

63-1305 AUTORADIOGRAPHIC STUDIES ON THE INCORPORATION OF LABELED PRECURSOR IN THE AH 130 ASCITES HEPATOMA CELLS AND IN THE LIVER FROM DAB-FED WISTAR RATS. (E.) Di Marco, A. (Dept. Exp. Biol., Natl. Inst. Stud. Cure Tumors, Milan, Italy), M. Gaetani and R. Silvestrini. *Acta Un. Int. Cancr.* 19(3-4):555-559, 1963.

In the liver of dimethylaminoazobenzene (DAB)-fed rats, early incorporation of tritiated uridine was observed only in the nuclear and nucleolar structures; radioactive RNA began to appear in the cytoplasm after many hr. At the same time the cytoplasmic radioactivity was higher in animals fed with DAB than in the controls. More detailed experiments were carried out in rats bearing ascites Hepatoma 130. All the nuclei of the interphase cells were labeled 16 min. after the i.p. inj. of the H^3 -uridine, while the radioactive RNA appeared in the cytoplasm only 1 hr. after the admin. of the precursor. Results support the hypothesis that in the cells of liver tumors, the nucleus is the site of RNA synthesis and that all the cytoplasmic RNA derives from the nucleus.

63-1306 CARCINOGENICITY AND METABOLISM OF 2-ACETYLAMINOFLUORENE IN THE RABBIT. (E.) Irving, C. C. (VA Med. Teach. Group Hosp., Memphis, Tenn.). *Acta Un. Int. Cancr.* 19(3-4):507-509, 1963.

The rate of hydroxylation of 2-acetylaminofluorene (AAF) by rabbit liver was one-half that reported for rat liver while the rate of deacetylation of AAF was approx. the same as that reported for rat liver. The kidney of the rabbit did hydroxylate and deacetylate AAF whereas rat kidney has no detectable hydroxylase or deacetylase activity. It has been shown that N-hydroxy-AAF is a major urinary metabolite of AAF in the rabbit. This metabolite was excreted as a conjugate cleaved by β -glucuronidase. These observations are important in view of the implication of N-hydroxy-AAF in the mechanism of AAF carcinogenesis in the rat.

63-1307 OZONOLYSIS OF POLYCYCLIC AROMATICS. X. 7,12-DIMETHYLBENZ[a]ANTHRACENE. (E.)

Moriconi, E. J. (Dept. Chem., Fordham U., New York) and L. B. Taranko. *J. Org. Chem.* 28(7): 1831-1834, 1963.

A study was made of the ozonization of 9,10-dimethyl-1,2-benzanthracene (DMBA) in methylene chloride, 3:1 methylene chloride-methanol, and acetone, and the products formed from oxidation of the resultant unstable peroxidic mixture. It appears that the L-region reactivity to ozone is decreased in the potent carcinogen DMBA, relative to 1,2-benzanthracene, while simultaneous K-region cleavage is increased as would be predicted from the Pullmans' K-region theory of carcinogenesis.

63-1308 PREPARATION OF CARCINOGENIC POLY-NUCLEAR HYDROCARBONS LABELLED WITH TRITIUM BY WILZBACH'S METHOD. (E.) Lijinsky, W. (Div. Oncol., Chicago Sch. Med., Ill.) and H. Garcia. *Nature (London)* 197:688-690, 1963.

The preparation of tritium-labeled 9,10-dimethyl-1,2-benzanthracene, 3,4-benzpyrene and 20-methyl-cholanthrene by the Wilzbach method is described. The distribution of tritium was studied by oxidation to known products and the loss of radioactivity was compared with that expected if the tritium were distributed randomly in the molecule.

63-1309 THE COMPARATIVE RADICAL REACTIVITY OF POLYCYCLIC AROMATIC HYDROCARBONS. (E.) Fell, G. S. (Dept. Cancer Res., Roy. Beatson Mem. Hosp., Glasgow, Scotland) and J. B. Spence. *Acta Un. Int. Cancr.* 19(3-4):497-498, 1963.

The comparative effects of thirteen polycyclic hydrocarbons (8 of the pyrene series, 5 anthracenes) in an *in vitro* system involving free radical species were studied. It was demonstrated that in a photochemical reaction some of the hydrocarbons could act as photosensitizing catalysts for the production of free radical species from a suitable labile source. Dibenzoyl peroxide was principally employed as a radical source and $\alpha\alpha$ -diphenylpicryl hydrazyl was used as an indicator for the rate of radical production. Investigations of the possible reaction mechanism indicated that an energy transfer process was involved and that this could be a general property of polycyclic hydrocarbons.

63-1310 A STUDY OF THE HISTOGENESIS OF EXPERIMENTAL MELANOTIC TUMORS RESEMBLING CELLULAR BLUE NEVI: THE EVIDENCE IN SUPPORT OF THEIR NEUROGENIC ORIGIN. (E.) Nakai, T. (Div. Oncol., Chicago Sch. Med., Ill.) and H. Rappaport. *Am. J. Path.* 43(2):175-199, 1963.

Further studies are reported on the histogenesis of melanotic tumors induced by 9,10-dimethyl-1,2-benzanthracene application to the skin of Syrian

golden and white hamsters. The neurofibroma-like pattern in many of the induced tumors and the observation of nerve fasciculi and small nerve fibers within the neoplasm first suggested the neurogenic origin of these experimental tumors. Electron microscopic studies revealed an abundance of myelinated and nonmyelinated nerves in the early melanotic lesions and a paucity of these structures in the advanced tumors. This was thought to be due to degeneration of nerve tissue which progressed as the tumors grew. Most significant was the observation of pigment granule formation in cells within the perineurium. Some of these cells had mesaxons and could therefore be identified as Schwann cells. Most of them were devoid of mesaxons and were therefore tentatively considered to be endoneurial cells even though they too might have been of Schwannian origin. The tumors exhibited strong nonspecific cholinesterase activity. This was also considered consistent with a neurogenic origin. (See also CRA 1(3):#376, 1963.)

63-1311 HETEROTRANSPLANTATION OF BLADDER CARCINOMA TO THE CHEEK POUCH OF THE SYRIAN HAMSTER. (E.) Peng, B. B. K. (Dept. Surg., State U. New York, Brooklyn), S. R. Weinberg and F. C. Hamm. *Investigat. Urol.* 1(1):76-82, 1963.

A method of heterotransplantation of bladder carcinoma to the hamster cheek pouch is described. Materials were derived from naturally occurring human bladder carcinoma and carcinogen-induced (β -naphthylamine) bladder carcinomas in dogs. The first and second generations of transplanted carcinomas were most difficult to induce. After the second generation, the growth rate of the human tumor increased with each transplantation; whereas the dog carcinogen-induced tumors regressed after the third generation of transplantation. Microscopically, the human tumor changed from transitional cell carcinoma to one with spindle cell features. This change became more pronounced with each transplantation. Chromosome studies have verified that these tumors are not spontaneous hamster tumors. No generalized metastases were found in any of the hamsters.

63-1312 EXPERIMENTAL CARCINOGENICITY AND ACUTE TOXICITY OF REPRESENTATIVE EPOXIDES. (E.) Weil, C. S. (Mellon Inst., Pittsburgh, Pa.), N. Condra, C. Haun and J. A. Striegel. *Am. Industr. Hyg. Assn. J.* 24(4):305-325, 1963.

Carcinogenic and acute toxicity potential were assayed while more than 60 epoxy compounds were being studied for commercial utility. Range-finding toxicity data are presented for 60, life time mouse skin-painting results are given for 24 and mouse sebaceous gland suppression results are listed for 26 compounds. Relationships discernible between molecular configuration and toxicity or irritation were tenuous at best. None of eleven monoepoxides produced tumors during lifetime

in painting of mice, while 5 of 17 diepoxides were tumorigenic (butadiene dioxide, vinylcyclohexene dioxide, bis-(2,3-epoxy-2-methylpropyl) ether, a methylcyclohexylmethyl ether, and a modified bis phenol diglycidyl ether). The latter duct was tumorigenic while both of its components were inactive when tested alone. The median latent period for tumor production was 15 to 23 months compared to 3-5 mo. for tumors produced by methylcholanthrene, used as a positive control. A relationship was observed between the suppression of sebaceous glands after a 2-wk. mouse skin-painting test, and tumor incidence in lifetime painting, but correlation was not sufficiently consistent to allow the brief test to be reliable for prediction of carcinogenic potential. No generalities about the toxic, irritative and carcinogenic hazards of handling epoxy compounds are justified by the presently known facts.

1313 LEYDIG CELL TUMOURS IN THE TESTES IMPLANTED TO FEMALE RATS. (Pol.)
K. (Dept. Biol. Tumors, Inst. Oncol.,
ie Sklodowska-Curie, Warsaw, Poland) and
Gadek. Nowotwory 13(2):113-123, 1963.

testes of newborn rats were implanted into
termate females; some of these females were
ovariectomized in mo. 2 of life. When examined
4 mo., there were no histological differences
the grafts of the ovariectomized and intact
ales. After 10 mo., Leydig cell tumors were
and in 4/5 ovariectomized females; in the fifth
there was hyperplasia of these cells. There
no tumors in 10 females with intact ovaries.
3 ovariectomized females Leydig cell tumors
eared in the testicular grafts as multiple
adenomatous nodules and in one female a
single nodule only was found in the graft. Some
nodules appearing within the same testis differed
morphologically from one another. They showed
ability to secrete estrogens and progesterone
was indicated by the characteristic histological
structure of the vagina, uterus and mammary glands.
Despite of these symptoms of the estrogenic
activity of Leydig cell tumors, typical castration
effects were found in the pituitary glands of the
rats.

1314 DO SOMATIC MUTATIONS INFLUENCE THE LIFE
SPAN OF MICE? (E., Abstract)
Kander, P. and D. I. Connell. Excerpta Med.
:26, 1963.

reduction in the expectation of life which
follows the exposure of mammals to ionizing
radiations has been attributed to the induction
of mutations in somatic cells. If this process
contributed significantly to the shortening of
life span, mutagenic chemicals would be expected
to bring about a similar effect. The monofunc-
tional alkylating agent, ethyl methanesulfonate
($\text{CH}_3\text{CH}_2\text{OSO}_2\text{CH}_3$) is an exceptionally powerful
mutagen, but unlike radiation and nitrogen mustards

is not cytotoxic to dividing cells. The admin-
istration of high doses of EMS had no effect on life span
although the effect of such treatments on spermatog-
enesis strongly indicates that the animal cells
were, in fact, subjected to mutagen action. EMS
induced kidney and lung tumors in CBA mice, but
these appeared so late in the life of the animal
that the life expectancy was not thereby signif-
icantly decreased.

63-1315 MALIGNANT RESPIRATORY TRACT NEOPLASMS
RELATED TO POISON GAS EXPOSURE. (E.)
Wada, S. (Dept. Int. Med., Hiroshima U. Sch. Med.,
Japan), Y. Nishimoto, M. Miyanishi, S. Katsuta,
M. Nishiki, A. Yamada, S. Tokuoka, H. Umisa and
M. Nagai. Hiroshima J. Med. Sci. 2(3):81-91,
1963.

See CRA 1(4):#641, 1963.

63-1316 METABOLISM OF BILE COMPONENTS DURING
HEPATOCARCINOGENESIS. I. CONJUGATION
OF CHOLIC ACID IN VITRO IN EXPERIMENTAL LIVER
CARCINOGENESIS. (E.) Songster, C. L. (Dept.
Path. Biochem., Tulane U. Sch. Med., New Orleans,
La.), S. S. Schochet, Jr. and E. Farber. Cancer
Res. 23(7):1069-1076, 1963.

The conjugation of cholic acid with taurine was
measured in liver microsomes and supernatant from
male rats (a) fed diets containing ethionine,
3'-methyl-dimethylaminoazobenzene (3'-Me-DAB),
or 2-acetylaminofluorene (2-AAF) or (b) subjected
to ligation of the common bile duct. A fairly
rapid decrease in in vitro conjugation was found
in the livers of the animals fed ethionine, be-
ginning 2 days after initiation, and reaching
a minimum value of less than 1% of the control
level within 10-14 days. The level of conjugation
returned to the control value within 10 days after
the ethionine was stopped. A similar defect was
not found in the livers of rats fed 3'-Me-DAB or
2-AAF under conditions which lead to the develop-
ment of liver cancer. Rats subjected to bile
duct ligation also showed no defect in tauro-
cholate synthesis. Since ethionine, 3'-Me-DAB,
2-AAF, and bile duct ligation all induce a similar
proliferation of bile duct epithelial cells, it
must be concluded that the defect in conjugation
of cholic acid with taurine cannot be of signifi-
cant importance as a biochemical basis for the
ductular proliferation.

63-1317 AZO DYES AND RAT LIVER GLUTATHIONE.
(E.) Neish, W. J. P. (Cancer Res. Unit,
U. Sheffield, Western Bank, England) and A. Rylett.
Biochem. Pharmacol. 12(8):893-903, 1963.

The level of male rat liver glutathione (GSH)
rapidly increased following i.p. inj. of 3'-methyl-
4-dimethylaminoazobenzene (3'-MeDAB). A more
gradual, less-pronounced increase resulted from
inj. of 4'-methyl-4-dimethylaminoazobenzene

(4'-MeDAB). On the contrary, 24 hr. after inj. of the non-carcinogenic azo dye, 2-methyl-4-dimethylaminoazobenzene, the level of rat liver GSH dropped below normal. In TCA extracts of 3'-MeDAB-treated liver, other changes occurred including an increase in phosphoethanolamine (PE). The pattern of changes was markedly similar to that observed by other workers in extracts of regenerating rat liver. The only marked change with the weak carcinogen 4'-MeDAB was the increase in GSH. A survey is given of substances capable of increasing liver GSH levels. These include the carcinogen 3,4,5,6-dibenzcarbazole, the anti-tumor agent, nitroimin and 2 anti-inflammatory agents (salicylic acid and antipyrine) which are not known to be carcinogenic. Attention is directed to the metal-chelating agent, 8-hydroxy-quinoline which has both anti-inflammatory properties and carcinogenic activity. It is suggested that anti-inflammatory substances should be carefully screened for carcinogenic and/or cocarcinogenic activity.

- 63-1318 VARIATIONS IN AMOUNTS OF TOBACCO TAR RETRIEVED FROM SELECTED MODELS OF SMOKING BEHAVIOR SIMULATED BY SMOKING MACHINE. (E.) Graham, S. (Dept. Epidemiol., Roswell Park Mem. Inst., Buffalo, N.Y.), S. Crouch, M. L. Levin and F. G. Bock. Cancer Res. 23(7):1025-1030, 1963.

Variations in human cigarette smoking habits suggested that examination by an analytic smoking machine be undertaken to discover whether yields of tobacco tar in simulations of these habits might differ. It was found in various experiments that: (a) Smoking a given number of puffs over a long period of time results in greater tar retrieval than smoking them over a short period. (b) Taking most of the puffs at the end of the cigarette results in the highest tar retrieval, puffing at regular intervals throughout the life of the cigarette gives the next largest yield, and taking most puffs at the beginning, the smallest retrieval. (c) Puffs taken at the end of a cigarette yield about twice the tar of puffs taken at the beginning.

- 63-1319 CHANGES OF MITOCHONDRIA AND THE ACTIVITY OF A NUMBER OF REDOX ENZYMES IN SPONTANEOUS AND CARCINOGEN-INDUCED TUMORS. (HISTOCHEMICAL EXAMINATION). (Rus.) Raikhlin, N. T. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). Ark. Pat. 25(7):24-32, 1963.

In a study of 125 malignant and 45 benign human tumors, of normal tissue as well as of tissues during the process of experimental carcinogenesis, the activity of succinic acid dehydrogenase, TPN-diaphorase, cytochrome oxidase and (inconstantly) of DPN-diaphorase and α -glycerophosphate dehydrogenase is decreased; the activity of

glucose-6-phosphate, 6-phosphogluconate, lactic and glutamic acid dehydrogenases is increased; the activity of malic and isocitric acid dehydrogenases shows almost no change. Mitochondria of normal and cancer cells react in response to the same unfavorable effects in a different way. Mitochondria of cancer cells prove to be more labile as compared to the normal, the permeability of the cancer cell membranes changes in the direction of easier penetration into the mitochondria of a number of substrates. Changes of the activity of a number of respiratory enzymes, detected in the cancer cells, may to some degree be connected with the physical peculiarities of mitochondria. During the early periods of experimental carcinogenesis, the histochemical detection of mitochondrial injuries (undetectable by other methods of investigation at that period) is possible.

- 63-1320 THE USE OF SEROTONIN, CHLORPROMAZINE AND OTHER AGENTS FOR CONDITIONING HOSTS FOR TUMOR HETEROTRANSPLANTATION. (E.) Olszewski, A. (Dept. Surg., Hahnemann Med. Coll., Philadelphia, Pa.), J. M. Howard and J. G. Strawitz. Am. J. Surg. 106(3):467-470, 1963.

Under the conditions of the experiment, serotonin conditions the rat to permit the heterotransplantation of the HEP III cancer. Chlorpromazine when given with irradiation or with irradiation and serotonin, resp., permitted the highest incidence of successful transplants and the largest tumors. After the third generation in the irradiation and serotonin combination, the tumor became progressively smaller. If the malignant cells were transplanted into an irradiation and cortisone-treated animal, the tumor took on renewed vitality.

- 63-1321 EFFECT OF CIGARETTE-SMOKE CONDENSATES ON HOMOGRAFTS OF EMBRYONIC LUNG TISSUE IN RATS. (E.) Hou, L. T. (Dept. Path., Sch. Med., Leeds, England) and R. A. Willis. J. Path. Bact. 86(1):199-207, 1963.

Experiments designed to test the possible, carcinogenic effects of cigarette tar and various fractions of it on s.c. and i.m. homografts of embryo lung in non-inbred rats are described. Of 1288 grafts, 644 with tarry material and 644 clean, 412 (229 contaminated and 183 clean) survived for periods ranging up to 600 days or more after implantation. Except for one small papilloma, none of the tar-containing grafts developed any tumors. 20-Methylcholanthrene pellets (3 parts to 1 part cholesterol) were placed in 56 grafts in rats which were killed or survived 200-558 days. Four developed highly differentiated squamous cell tumors, one of which was certainly cancerous; 18 host rats developed sarcomas at the graft sites.

1322 20-METHYLCHOLANTHRENE CARCINOGENESIS IN THE SKIN OF PITUITARY DWARF MICE. DIFFERENTIATION OF OUTCOME AT FULL LIFE SPANS BY MATOTROPIC GROWTH HORMONE ADMINISTRATION. (Abstract) Campbell, J. S., P. Fournier and Mott. Excerpta Med. (57):9, 1963.

Minimal 20-methylcholanthrene (MC) dosages to cause skin produced epidermal dysplasias after about 90 days, when keratoacanthomas, cutaneous ulcers, leukoplakia and "senile" keratoses appeared. Malignancy ensued late. Five of 15 pituitary dwarf mice surviving mean periods of 214 days following MC developed epidermoid carcinoma. After STH admin., one group of 8 pituitary dwarf mice survived a mean period of 278 experimental days; 4 of these mice developed skin cancer, as did 13 of 28 MC-treated phenotypically normal pituitary dwarf mice, 7 out of 10 STH-treated control mice and 10 out of 13 control mice not treated by STH developed epidermoid skin cancer. Induced skin cancers were more frequent in STH-treated pituitary dwarf mice than in pituitary dwarf mice not treated by STH. The data would indicate this difference to prolongation of life spans by correction of hormonal deficits rather than to neoplastic promotion by STH. Here, a threshold rather than "bombardment" MC dosages were employed, carcinogenesis was characteristic only of rather aged skins.

1323 EFFECT OF AUDIOGENIC STRESS UPON 20-METHYLCHOLANTHRENE-INDUCED CARCINOGENESIS IN MICE. (E.) Molomut, N. (Waldemar Res. Found., Inc., Port Washington, N.Y.), Lazere and L. W. Smith. Cancer Res. 23(7):7-1101, 1963.

DBA/1 (audiogenic seizure-susceptible) and A/Jax (seizure-resistant) mice were subjected to a 10-day ringing sound and an approx. 80-90% effective carcinogenic dose of 20-methylcholanthrene and observed for time of tumor induction and ultimate survival. There was a delay in the time of tumor induction (latent period) in DBA/1 mice subjected to audio stimulus as compared with DBA/1 controls, whereas A/Jax mice were unaffected. Despite the delayed tumor induction in sound-treated DBA/1 mice, their survival time was the same as comparable controls. It is believed that, once induced, the tumor cell growth was not inhibited by the sound stress exposure. No significant differences in carcinogenesis were observed when cortisone was admin. in lieu of sound stress. The addition of cortisone to sound stress exposure significantly reduced the tumor induction in the DBA/1 mice (58%), whereas tumor induction in A/Jax mice was 100%, a slight decrease over A/Jax controls.

1324 CHLORINATION OF DRINKING WATER AND 3,4-BENZOPYRENE. (Ger.) Gräf, W. (Inst. Hygiene-Bacteriol., Friedrich-Alexander-Universität Erlangen, Germany) and C. Nothhaft.

Arch. Hyg. Bakt. 147(2-3):135-146, 1963.

The effect of chlorination of drinking water upon small quantities of added 3,4-benzpyrene (BP; 2 and 5 µg/liter) was investigated. BP is continuously decreased as a function of the reaction time. The decrease is logarithmic with a half period of from 2-3 hr. In the case of the 2 µg/liter conc. the BP disappears completely only after 12-13 hr., while about 20% of the original quantity remains even after 22 hr. in the 5 µg/liter soln. With the decrease of the BP two new reaction products appear: 5-monochloro-3,4-benzpyrene and 3,4-benzpyrene-5,8-quinone. Of these two compounds, the 5-monochloro-benzpyrene is produced in the greater amount and probably retains its carcinogenic properties; benzpyrene-5,8-quinone is no longer capable of inducing tumors.

63-1325 ABSORPTION AND EXCRETION OF BENZOPYRENE. OBSERVATIONS IN THE DUCK, CHICKEN, MOUSE AND DOG. (E.) Rigdon, R. H. (Dept. Path., U. Texas Med. Br., Galveston) and J. Neal. Texas Rep. Biol. Med. 21(2):247-261, 1963.

Large amounts of 3,4-benzpyrene (BP) crystals and/or BP suspended in a physiologic soln. of sodium chloride with a 1% soln. of polysorbate 80 have been given orally to ducks, chickens, mice and dogs and intratracheally to ducks with no noticeable acute injurious effect. BP has been demonstrated spectrophotometrically in the blood and bile of chickens and dogs and in the blood of the duck. The presence of this hydrocarbon in the blood and bile is influenced by the interval elapsing between the inj. of the BP and the time the sample was obtained. The skin of the chicken and mouse has a definite blue fluorescence with UV light following oral admin. of BP. The mesentery, gallbladder, kidney and urine of the mice fluoresce. The kidney of the chicken and duck likewise fluoresces.

63-1326 REACTION OF THE PERITONEAL MESOTHELIUM OF THE RAT TO IRRITANTS: A CYTOHISTOLOGIC STUDY. (E.) Hoda, M. N. (Dept. Path., Postgrad. Med. Ctr., Karachi, Pakistan) and H. Zaman. Acta Cytol. (Phila.) 7(4):252-257, 1963.

The reactions of the peritoneal mesothelium to the i.p. introduction of three different irritants, viz., a 50% saline suspension of aluminum hydroxide, a 25% suspension of magnesium silicate and a 20-methylcholanthrene-beeswax-impregnated thread were studied in rats. Examination of smears prepared from the peritoneal washings did not reveal any marked degree of atypism suggestive of malignancy. A study of the percentage distribution of 3 different types of mesothelial cells revealed no correlation with the type of inflammatory process produced.

63-1327 FINE STRUCTURAL CHANGES IN MOUSE CERVICAL EPITHELIUM FOLLOWING METHYLCHOLANTHRENE. (E., Abstract) Schrodtt, G. R. (U. Louisville Sch. Med., Ky.). Am. J. Path. 43(1):41a, 1963.

20-Methylcholanthrene was applied to the cervix of C3H mice tri-weekly under direct visualization. Animals were sacrificed in pairs at regular intervals after up to 58 paintings; at this time grossly invasive tumors were observed. Low magnification electron microscopy demonstrated nuclear and overall cellular changes which corresponded with light microscopic observations. The number of electron-dense cytoplasmic structures resembling lysosomes increased in number after repeated applications of the carcinogen, but before the stage of invasive cancer. Mitochondrial alterations were noted at the stage of so-called dysplasia, and were quite prominent in the invasive cancers. In many mitochondria one or several round homogeneous electron-dense bodies were present. At the present time the significance of these changes is not known.

63-1328 A HISTOCHEMICAL STUDY OF SUCCINIC DEHYDROGENASE ACTIVITY IN RAT LIVER CANCEROGENESIS INDUCED BY 3-METHYL-4-DIMETHYL-AMINOAZOBENZENE. (E.) Hadjiolov, D. C. (Dept. Path., Oncol. Res. Inst., Sofia, Bulgaria). Experientia 19(6):316-317, 1963.

Albino rats fed a semi-synthetic diet containing 0.06% 3-methyl-4-dimethylaminoazobenzene were killed at intervals from 15-150 days from start of treatment. The results indicate that in the course of azo-dye-induced rat liver carcinogenesis the succinic dehydrogenase activity in parenchyma and bile duct cells follows a definite pattern. In hepatoma it is markedly lower than in both normal parenchymal cells and hyperplastic parenchymal cell nodules. The negative reaction seen in normal bile duct cells becomes positive in cholangiofibrosis and cholangiomas with a possible subsequent decrease in more dedifferentiated cholangiocarcinomas.

63-1329 A MOLECULAR APPROACH TO TERATOGENESIS: EFFECT OF VITAMIN A ON INFLUENZA VIRUS IN OVO. (E.) Blough, H. A. (Dept. Path., U. Cambridge, England). Nature (London) 199:33-35, 1963.

Influenza A virus (strain PR8) was inoc. into eggs, and treated 6 hr. later with 5-150 µg of various vitamin A derivatives (alcohol, all-trans aldehyde, acetate or acid). Upon electron microscope examination the vitamin-treated virus showed marked pleomorphism, with the filamentous forms most prevalent. With 150 µg of all vitamin A preparations, 10-12% were aberrant forms (>200 mµ in diameter). In some cases large portions of the viral envelope was dissolved revealing a tightly bound internal helix. In contrast to the effect of saponin on the Rous sarcoma virus *in vitro* hexagonal arrays were not observed. Infectivity and hemagglutination titers were little changed suggesting that the nucleoprotein helix was unchanged. It is suggested that vitamin A exerts its teratogenic effect by a direct physico-chemical attack on the cell membrane.

63-1330 THE INFLUENCE OF METHYLCHOLANTHRENE ON OXYGEN CONSUMPTION. (E.) O'Connor, P. (Dept. Path., University Coll., Dublin, Ireland). Irish J. Med. Sci. 6(450):271-278, 1963.

A respirometer was used to determine O₂ consumption in random bred mice. With 9 control mice at a temperature range varying from 39-30°C, there was demonstrated the presence of three oxygen peaks occurring at 36.3, 34.7, and 30.7°C, attributable to the presence of palmitic, myristic, and lauric acids, resp. Mice that were painted with 20-methylcholanthrene (2x/wk. x 4), tended to show a displacement of 2 of these normally occurring oxygen peaks, to a temperature range below 30°C. When topical applications of myristic acid or palmitic acid were alternated with 20-Me, the peaks of oxygen consumption again showed a downward shift.

See also abstract nos.: 1219, 1224, 1225, 1226, 1232, 1376, 1380, 1387, 1388, 1389

VIRAL CARCINOGENESIS

1331 EFFECT OF X-IRRADIATION ON THE DEVELOPMENT OF FRIEND DISEASE. (Fr.) Lan, J. F. (Pasteur Lab. Radium Inst., Paris) C. Levy. Bull. Assn. Franc. Cancer 49(4):398, 1962.

Female mice were inoc. at 10 days with cell-free extracts from spleens of mice with Friend leukemia (0.2 ml of a 25% homogenate in saline, i.p.) and irradiated (300 r) at 40 days. Irradiated and nonirradiated mice developed leukemia, but in 3 separate experiments the survival of mice receiving total body irradiation plus splenic irradiation (through exteriorization of the spleen) was prolonged significantly over nonirradiated controls: 60-105.3 and 72.3-157 days, resp., controls 47-85.6 days. However, when mice were irradiated and then 3, 5, or 6 days later were inoc. with the leukemic extracts, survival time did not differ significantly except for a possible slight prolongation of survival in totally irradiated mice receiving splenic irradiation 3 days prior to virus inoc. Study of peripheral blood, marrow and other organs of mice inoc. with Friend leukemia at 10 days, and irradiated 30 days later showed in nonirradiated animals leukopenia and erythrocytopenia of about 10 days duration. The spleen exhibited transient destruction of lymphoid, myeloid and erythroblastic cells, but not of Friend cells; and by 4-6 days, spleens resembled those of nonirradiated controls. However about 10 days after irradiation the livers showed nearly complete infiltration by Friend cells. Survival of mice inoc. 39 days previously with Friend virus, when inoc. into newborn mice, was reduced in 11/12 mice with a mean survival of 30 days when donors were spleen-irradiated 9 days before; in 8/12 mice with a mean survival of 36 days when from totally irradiated donors; and in 11/12 with a mean survival of 28 days when from nonirradiated controls. Results suggest that total body irradiation has a depressing effect on the development of Friend leukemia, whereas the effect of splenic irradiation is merely a secondary result due to operative trauma with consequent spread of tumor cells to the liver.

1332 ORIGIN AND TRANSMISSION OF FRIEND LEUKEMIA. (Fr.) Chamorro, A. (Pasteur Lab. Radium Inst., Paris). Bull. Assn. Franc. Cancer 49(4):399-415, 1962.

A study of the origin and transmission of Friend leukemia, sera and cell-free extracts from the healthy and diseased organs of Swiss and albino breeder and Swiss virgin mice were injected. Swiss mice aged 1-75 days. Two strains of Friend leukemia were isolated. Strain R-2 was from a retired breeder, aged 14 mo., with a small parathyroid adenoma, a spleen wt. of 2575 mg, and a liver wt. of 7044 mg with many whitish nodules

resembling early stages of Friend cell infiltration. When inoc. (i.p.) with 0.2 ml of serum, 3/3 26-day-old mice developed leukemia; after 0.2 ml of an organ extract, 4/6 30-day-old mice also developed leukemia. The serum (0.1 ml i.p.) of the other strain, LS 2 (from a virgin female aged 10 mo., with lymphatic leukemia and lymphoid infiltration of the kidney and spleen) induced leukemia in 3/3 10-day-old mice but organ extracts were ineffective. Continuous passage of these 2 strains using either serum or cell-free extracts of affected organs gave consistent strain specific differences. In 63 mice inoc. with R-2, there were 60% takes, with a latency of 30-45 days. In 19 inoc. with strain LS 2 takes were 100%, with a latency of 10-15 days. Females injected i.p. with active extracts during pregnancy did not transmit the agent to the fetuses. When injected after parturition, agent was not transmitted in the milk. Crosses between a diseased and/or healthy or diseased parent of Swiss, XVII and RIII crosses led to no leukemia in the offspring at 75 days. Among surviving offspring, 32 (42.5%) developed leukemias (17 Friend, 10 myeloid and 5 chloroleukemias). While the distribution of leukemia types was not affected, there were distinct strain differences. On second passage there was a sharp decrease in the frequency of myeloid and chloroleukemias in the F2 from 3 Friend-, and 4 LS 2-infected parents. The F2 showed an increased latency for Friend leukemia (4-10 mo.) and a decrease or absence of Friend cells in the peripheral blood.

63-1333 SPECIFICITY OF VIRUS-INDUCED RESISTANCE TO TRANSPLANTATION OF POLYOMA AND SV40 TUMORS IN ADULT HAMSTERS. (E.) Koch, M. A. (Child. Hosp. Res. Found., U. Cincinnati Coll. Med., Ohio) and A. B. Sabin. Proc. Soc. Exp. Biol. Med. 113(1):4-12, 1963.

Specificity of the transplantation resistance phenomenon was tested by using only 10 tissue cultured polyoma (P), SV40 and F.Sa.No.3B (FSB) hamster tumor cells (TC) in large numbers of adult hamsters. Pre-treatment with P virus (V) regularly produced resistance to transplantation of P TC but not of FSB TC; there was evidence of some resistance to SV40 TC in only 2/4 tests. Pre-treatment with SV40 regularly produced resistance to SV40 TC (although in some tests of a lower order than in the PV P tumor system) but not to FSB cells; there was evidence of some resistance to P TC in only 2/4 tests. Pre-treatment with adenoviruses, types 12 and 7A, herpes virus and poliovirus type 1 produced no resistance against any of the 3 tumors. Reovirus, type 3, and vesicular stomatitis virus (Indiana strain) propagated in mouse embryo tissue culture (the same cells in which the PV was grown) produced no resistance against the P TC. The progeny of 10 P hamster TC which formed large tumors in occasional, polyoma-immune adult hamsters, nevertheless, were shown to possess the distinctive,

cellular antigen. A sensitive test failed to reveal any cytotoxic antibody in the serum of polyoma-immune hamsters that resisted transplantation of P TC.

63-1334 EFFECT OF SV40 VIRUS IMMUNIZATION ON GROWTH OF TRANSPLANTABLE SV40 AND POLYOMA VIRUS TUMORS IN HAMSTERS. (E.)

Defendi, V. (Wistar Inst. Anat. Biol., Philadelphia, Pa.). *Proc. Soc. Exp. Biol. Med.* 113(1): 12-16, 1963.

Adult hamsters immunized with SV40 or polyoma virus (PV), when challenged with graded doses of virus-free polyoma or SV40 tumor cells, were resistant to small inoculums of cultured cells from tumors originally produced by the same viruses. There was no cross protection between PV immunization and SV40 tumor cells or between SV40 virus immunization and polyoma tumor cells, even at the minimum cell dose required to give tumors in all the animals.

63-1335 EFFECTS OF DEUTERIUM OXIDE UPON PLAQUE FORMATION AND REPLICATION OF SIMIAN VIRUS 40. (E.)

Carp, R. I. (Wistar Inst. Anat. Biol., Philadelphia, Pa.), I. Chudnow, H. Koprowski and D. Kritchevsky. *Proc. Soc. Exp. Biol. Med.* 113(3):569-571, 1963.

The influence of D₂O (25 and 50%) upon multiplication of and plaque formation by simian virus 40 (SV40) was studied *in vitro* in Grivet monkey kidney tissue at 37°C and 40°C. At both temperatures the presence of 25-50% of D₂O in the growth medium resulted in reduced virus yield, lower endpoint titer and reduced plaque size. When the SV40 virus was incubated at 37°C with 25% of D₂O in the medium, there was no inactivation after 8 days.

63-1336 TRANSFORMATION OF CHINESE HAMSTER EMBRYONAL DERIVATIVES WITH POLYOMA AND SV40 VIRUSES. (E., Abstract) Yerganian, G. (Child. Cancer Res. Found., Boston, Mass.). *Genetics* 48(7):917, 1963.

Secondary cultures from 18-day-old hamster embryos exposed to 0.1 ml of 10¹⁰ PFU/ml (small plaque) polyoma virus (PV) resulted in the transformation and rapid proliferation of morphologically distinct cell types. Analysis of 8 representative focal lines (360 metaphases) showed an av. of 75% classic diploidy, 14% classic tetraploidy, and 11% aneuploidy. Clones retained even higher percentages of classic diploidy and their plating efficiencies ranged from 13-39%. SV40-transformed lines (30-60 days old) exhibited multilayering of otherwise normal-appearing fibroblast-like clones, in addition to ruffling of the cytoplasmic edges of peripheral cells. The chromosomes of the PV-transformed lines are considered to be the best yet to be observed among experi-

mental lines of this species, especially since the secondary constrictions of both X's are extremely clear. SV40-transformed lines were readily overspiralized during comparable exposure to colchicine, a feature which may serve as a marker when both viruses are employed simultaneously.

63-1337 STRUCTURE OF SOME SIMIAN ADENOVIRUSES. (E.) Archetti, I. (Lab. Microbiol., Inst. Superiore Sanita, Rome, Italy) and D. Steve-Bocciarelli. *Virology* 20(3):399-404, 1963.

A group of simian adenoviruses (SV1, SV20, SV23, SV11, SV34, and SV39) were grown in monkey kidney cells, purified and examined under the electron microscope. Most observations were done on unfixed viruses, and were seen in negative contrast produced by PTA. All were about 80 mμ in size and had an internal core about 45 mμ in diameter. The external shell was icosahedral in shape and built from 252 morphological components (capsomeres) which looked identical and were uniform in arrangement. The strains were all quite similar to adenovirus type 5 described by Horne et al. The capsomeres showed evidence of being built from 5 small subunits 2-3 mμ in diameter. Elongated forms, apparently helical in shape, may be aggregates of scattered capsomeres.

63-1338 THE DEVELOPMENT OF LEUKEMIA AND TUMORS IN AN EXPERIMENT ON MICE OF THE C3HA LINE. (E.) Parnes, V. A. (N. F. Gamaleya Inst. Epidemiol. Microbiol., Acad. Med. Sci. USSR, Moscow) and A. G. Varshavskii. *Biull. Eksp. Biol. Med.* (Eng.) 53(3):307-310, 1963.

Fluid from passages 3 and 5 of monkey kidney tissue cultures originally inj. with blood from a pt. with acute leukemia (hemocytoblastosis), when inj. into newborn CC57 mice produced no pathological changes. Fluid from passage 7 inj. i.p. into 1-day-old C3HA mice resulted in death of all 10 after 2 mo.; similar fluid inj. s.c. and i.p. in 4-day-old mice resulted in 4/6 deaths after 6 wk. with signs of lymph node enlargement. The remaining 2 mice were sacrificed after 7 wk. Inj. (s.c.) of material from these mice into 22-day-old C3HA mice resulted in no neoplasms after 8.5 mo; when inj. i.p. into 1-month-old mice, neoplasms developed at approx. ages of 4, 5 and 11 mo. All developed enlarged spleen, liver and large cysts, with palpable tumor in 2 mice and enlarged lymph nodes in the other. Material from the tumor-bearing mice was serially passaged in mice of the same strain. When tumor tissue from passage 6 was inj. into newborn Afb mice, symptoms of generalized leukemia developed and tumor nodules were found at the site of inj.; death occurred after 1.5 mo. Material from passages 10 and 16 was successfully transferred to CC57 brown and C3H(f) mice.

1339 TUMORS INDUCED IN PRIMATES BY CHICKEN SARCOMA. (E., Abstract) Munroe, J. S. (Loan-Kettering Inst. Cancer Res., New York). *Physiologist* 6(3):240, 1963.

The Zilber strain of Rous sarcoma virus was inj. to adult and newborn rhesus monkeys. One adult was killed for study; none of the remaining 3 but for 13 wk. developed tumors. One premature died 6 days after inj. of a tumor suspension to the wing web; virus was demonstrated in the thigh and liver. Another was killed 6 days after inj. of a cell-free filtrate. All the remaining developed tumors; 3 were histologically fibrosarcomas. One tumor which appeared 6 wk. after inoc. was excised for study but recurred in 14 days. In 2 newborn monkeys fast-growing tumors appeared after 3 wk. and the animals were killed because of debility. In these tumors virus was demonstrable by 3 serial passages in chicks. Immaturity of immunity mechanisms in the monkey at birth may account for crossing the species barrier from bird to primate.

1340 ON THE PATHOGENESIS OF CYSTIC LYMPHADENOPATHY OF RATS DUE TO ROUS SARCOMA VIRUS. (Rus.) Shapiro, V. S. (N.F. Gamaleya Inst. Epidem. Microbiol., Acad. Med. Sci. USSR, Moscow) and T. D. Morgunova. *Vop. Virus* 8(3):5-348, 1963.

The supernatant of a previously frozen Rous sarcoma ground with sand and with the addition of 1% hyaluronidase and saline (virus titer 1:5,000) was inj. s.c. into newborn Wistar rats over a period of 4 days in a total dose of 1.5 cc. Animals were killed at 2-day intervals from day 5-40. Histological examination of the axillary, radial, neck and inguinal lymph nodes during the precystic stage revealed proliferation of reticular cells with a large number in active mitosis. Dilatation of nodular sinuses and rarefaction of the lymphatic tissue was also observed. This was followed by hyperplasia and hypertrophy of the reticular cells lining the sinuses and hypertrophied elements in the follicles and medullary cords. Desquamation of eosinophilic reticular macrophages and their passage into the lumen of the dilated sinuses was also observed. The next step in the formation of the cyst was rarefaction of the reticular tissue and destruction of the remaining parenchyma.

1341 SPONTANEOUS TUMORS IN GERM-FREE RATS. (E.) Pollard, M. (Lobund Lab. Dept. Biol., U. Notre Dame, Indiana) and B. A. Teah. *Nat. Cancer Inst.* 31(2):457-465, 1963.

Germfree rats derived from Fischer and Sprague-Dawley stock maintained for 3 and 2 yr., resp., have shown no spontaneous tumors. Among germfree rats derived from the Wistar strain and maintained for 8 yr., 25 tumors have been observed, the majority of which involved the mammary gland. By present methods of study no

microbiol or viral agents have been isolated. An eosinophilic intranuclear inclusion body was observed in the acinar cells of the lacrimal glands of adult germfree males; inclusion bodies were noted in lacrimal glands of adult Fischer and Sprague-Dawley males. A similar inclusion has been noted in the lacrimal glands of 30 conventional male rats. The enlarged cecum was noted in all germfree animals.

63-1342 STUDIES ON SL MOUSE LEUKEMIA. IV. CELL-FREE TRANSMISSION. (Jap.) Ichikawa, Y. (Dept. Pathol., Inst. Virus Res., Kyoto U., Japan). *Nippon Keitsueki Gakkai Zasshi (Acta Haemat. Jap.)* 25(5):743-751, 1962.

Cell-free extracts of leukemic tissues of SL mice were investigated for the existence of a leukemogenic agent capable of inducing leukemia in non-leukemic S strain mice. After serial passages in S mice, this agent became highly potent not only in newborn but suckling and adult mice as well. Leukemia incidences in the latter 2 groups were 32.8 and 30.8%, resp. In general, female mice showed 2-3 times greater susceptibility than male mice, and shorter survival times following inoc.

63-1343 LEUKEMOGENIC ACTIVITY OF CELL-FREE FILTRATES FROM RADIATION-INDUCED LEUKEMIA OF RF MICE. (Jap.) Hiraki, K. (Dept. Intern. Med., Okayama U. Sch. Med., Japan), S. Irino, S. Sota and K. Ikejiri. *Nippon Keitsueki Gakkai Zasshi (Acta Haemat. Jap.)* 25(6):816-821, 1962.

Incidence of leukemia in RF mice exposed to a single dose of whole body X-irradiation (350 r) was 77.4% of 53. As to type, 20 developed thymic, 20 non-thymic lymphocytic leukemia while only 1 developed myelogenous leukemia. When cell-free filtrates from these leukemic mice were inoc. into newborn mice of the same strain (less than 16 hr. old), 2/12 developed leukemia after 357 and 374 days. Similar inoc. of newborn mice with cell-free filtrates from normal mice did not produce leukemia and no non-irradiated animals developed leukemia.

63-1344 ON THE POSSIBILITY OF ELEVATING THE BIOLOGICAL ACTIVITY OF EXTRACTS FROM HUMAN LEUKEMIC TISSUE. (E.) Dement'eva, V. (P.A. Gertsen State Sci. Res. Inst. Oncol., Moscow) and V. M. Bergol'ts. *Biull. Eksp. Biol. Med. (Eng.)* 53(3):311-312, 1963.

Equal parts of supernatants of both untreated and heat-inactivated homogenates (diluted 1:5 with saline) of brain and spleen of a pt. who died of acute hemocytoblastosis, were inj. in various combinations (sometimes with hyaluronidase) into the brain of 4-week-old C3HA mice or into the thymus of random bred mice 20-22 days of age. Greatest number of leukemias resulted from inj. into the thymus of untreated spleen + untreated brain + hyaluronidase (7/10 mice that survived

2 mo.). When the hyaluronidase was omitted, 3/9 that survived 2 mo. developed leukemia; av. latent period was 5 mo. Thymus inj. of untreated brain and inactivated spleen extract led to 2/10 with leukemia, and av. latent period was 4.5 mo. Inj. of both untreated and inactivated brain extract had little effect (1/10 with leukemia). In mice which received the inj. into the brain, no leukemias appeared in groups of 12 and 14 after treatment with inactivated brain + untreated spleen and both untreated and inactivated spleen, resp.

63-1345 MORPHOLOGIC CHANGES PRECEDING VIRUS-INDUCED LEUKEMIA IN RODENTS. (E.)

Dunn, T. B. (NCI, Bethesda). Acta Un. Int. Cancr. 19(3-4):665-667, 1963.

When BALB/c mice given the Moloney virus were thymectomized or splenectomized or subjected to both procedures, the incidence of lymphocytic leukemia was reduced. However, other forms of reticular neoplasms appeared in greater numbers than are found in intact BALB/c mice. Mice given the Rauscher virus show increased proliferation of blood-forming tissues before lymphocytic leukemia develops in the thymus.

63-1346 RESISTANCE AND SUSCEPTIBILITY TO CHALLENGE INFECTION OF POLYOMA-INDUCED TUMOR CELL CLONES. (E.) Gershon, D. (Lab. Virol. Genet., Weizmann Inst. Sci., Rehovoth, Israel) and L. Sachs. Virology 20(4):567-576, 1963.

Resistance to challenge infection with polyoma virus (PV) was studied in 77 clones derived from a PV-induced mouse mammary tumor and in 9 clones derived from a PV-induced mouse parotid tumor clone. There was no spontaneous virus production at any time. Cloning of 2 uncloned resistant mass populations of the mammary tumor yielded 55% susceptible clones, while cloning of 2 susceptible clones derived from this tumor yielded 7% and 37% resistant clones. The derivation of resistant from susceptible clones was observed through 2 cycles of recloning. Although the uncloned resistant populations thus gave rise to susceptible clones, and susceptible clones gave rise to resistant clones, resistant clones derived from the mammary and parotid tumor produced only resistant clones. Two susceptible clones and an uncloned susceptible mass population became resistant after a series of transplantations in mice, a result suggesting a selective advantage for resistant cells *in vivo*. PV-inoculation of the grafted mice inhibited *in vivo* growth after cell grafting, both with a resistant and a susceptible clone. There was no apparent correlation between observed differences in the karyotypes of the tumor cells and their reaction to challenge infection. Clones of PV-induced tumors that were resistant to PV challenge infection supported multiplication of mouse encephalomyocarditis virus. It is concluded that resistance of PV-induced

tumor cells to PV challenge infection differs in some respects from the immunity of lysogenic bacteria to superinfection.

63-1347 ATTEMPTED CULTURE OF THE VIRUS OF THE MOUSE MYELOID LEUKEMIA. (Ger., Thesis, Fac. Math. Sci., Humboldt U., Berlin.) Baumbach, Wiss. Zschr. Humboldt Univ. Berlin (Math. Naturwiss.) 12(2):301, 1963.

Repeated inoc. of mice with cell-free filtrate of the culture medium of leukemic lymph nodes explants kept in plasma cultures for 3 to 5 mo. led to the development of leukemias after an av. latent period of 2 to 6 mo., corresponding largely both hematologically and histologically to the initial type. Experiments on the culture of this virus in trypsinized mouse embryonal tissue demonstrated a transmissible cytopathogenic effect leading to the occurrence of various tumors in mice, rats and hamsters. These results indicate that not only is a culture of the leukemia virus being dealt with, but that an activation and multiplication of a second virus (BBT₂), belonging to the polyoma group, had taken place. The tumors produced by this virus in mice were characterized as mesenchymal tumors.

63-1348 WOUND-TUMOR VIRUS ANTIGENS IN THE INTERNAL ORGANS OF AN INSECT VECTOR. (E.) Sinha, R. C. (Dept. Bot., U. Illinois, Urbana) and L. M. Black. Virology 21(2):183-187, 1963.

Wound-tumor virus antigens were detected in hemolymph smears of viruliferous leafhoppers (Agallia constricta) of both sexes, and in smears of the fat body from female transmitters, by using fluorescent antibodies. When organs of the same kind from 11-20 exposed or viruliferous leafhoppers were pooled and extracts tested for wound-tumor soluble antigens by the precipitin ring test, a positive reaction was given by the fat body, intestine, and salivary glands of both sexes and by the ovaries. While the highest conc. was in the fat body, it seems probable that the initial site of infection is the intestinal tract.

63-1349 IN UTERO TRANSMISSION OF THE MOUSE MAMMARY TUMOR AGENT. (E.) Andervont, H. B. (NCI, Bethesda). J. Nat. Cancer Inst. 31(2):261-272, 1963.

Transmission of the mammary tumor agent of the male parent was studied by mating 25 agent-free strain BALB/c female mice to agent-carrying strain C3H males to procure F1 hybrids. The F1 hybrid females were bred to agent-free strain C3H males to obtain first-generation backcross mice and these females were also bred to agent-free C3H males to supply second backcross progeny. Thus, 2 backcross generations served as "progeny test" mice for the presence of the agent in their female

hybrid or BALB/c ancestor. The C3H father's parent gained access to the descendants of 6 BALB/c females. In 4 families the father's parent infected the BALB/c female because thereafter all F1 hybrids and their backcross progeny developed mammary tumors. In the fifth family F1 hybrids of the third litter and their backcross descendants carried the agent, whereas an littermate and her descendants did not. An hybrid of the 4th litter and her descendants were also free from the agent. In the 6th family 4 F1 hybrids of the third litter and their descendants were infected, but in the 4th litter only 1 of 3 F1 hybrids was infected. A hybrid of the fifth litter was not infected. The last 2 families suggest in utero infection of the F1 hybrids without concomitant infection of their BALB/c mother.

63-1350 DETECTION OF AN AVIRULENT VIRUS APPARENTLY RELATED TO FRIEND VIRUS. (E.) Pope, J. H. (Queensland Inst. Med. Res., Brisbane, Australia). Aust. J. Exp. Biol. Med. 41(4):349-361, 1963.

The WMI-B strain of Friend virus was originally recovered from mice which had been inoculated with Friend virus. Antisera prepared in stock C3H mice against either WMI-B or WMI virus neutralized WMI-B virus but not WMI virus. Q.I.M.R. mice infected with WMI virus were resistant to superinfection with WMI-B virus. By treatment of WMI-B virus with C3H antiserum to WMI virus, a strain of WMI virus was obtained which did not induce antibodies to WMI-B virus in C3H mice and did not protect Q.I.M.R. mice against challenge with WMI-B virus, but which did produce the lymphoid hyperplasia typical of WMI virus infection. This pure WMI strain was still of relationship to WMI-B virus at the 8th passage. The original WMI line therefore contained two viruses. One (WMI virus) caused lymphoid hyperplasia in Q.I.M.R. mice, while the other (an avirulent variant of WMI-B virus) caused signs but was detectable by means of neutralization and protection tests. Seventeen wild mice were studied virologically. Strains of virus resembling pure WMI virus were isolated from two wild mice, and an avirulent strain related to WMI-B virus was obtained from a third, while both viruses were isolated from three other wild mice. It was concluded that an avirulent virus, which is apparently related to Friend virus, occurs in wild mice in Queensland.

63-1351 ATTEMPTS TO TRANSFER THE MAMMARY TUMOUR AGENT FROM INFECTED MALE MICE TO SUSCEPTIBLE NEW-BORN FEMALES. (E.) Peacock, A. (Royal Beatson Mem. Hosp., Glasgow, Scotland). Brit. J. Cancer 17(2):252-254, 1963.

virus free RIIIf/Pu male and one or two of its litter mate sisters were mated in the same cage and from this time spent their lives below a cage in which was housed a C3H mammary tumor

agent (MTA) virus carrying male. A wire netting floor allowed droppings to fall freely into the cage directly below, but no contact was possible between the C3H and RIIIf/Pu mice. Despite prolonged contamination by excreta and bodily secretions of the MTA positive C3H males, there was no increase in the incidence of mammary tumors in susceptible newborn RIIIf/Pu females or their mothers.

63-1352 ELECTRON MICROSCOPIC STUDY OF HUMAN LARYNGEAL PAPILLOMATOSIS. (E.) Svoboda, D. J. (Dept. Path. Oncol., U. Kansas Med. Ctr., Kansas City), F. R. Kirchner and G. O. Proud. Cancer Res. 23(7):1084-1089, 1963.

Electron microscopic examination of cytoplasmic bodies in human laryngeal papillomas revealed them to consist of membrane-bound cell remnants such as mitochondria, lipids, endoplasmic reticulum and nucleus. No viral particles were detected.

63-1353 FORMATION OF CYTOTOXIC ANTIBODY AGAINST LEUKEMIAS INDUCED BY FRIEND VIRUS. (E.) Old, L. J. (Sloan-Kettering Inst. Cancer Res., New York), E. A. Boyse and F. Lilly. Cancer Res. 23(7):1063-1068, 1963.

A specific antigenic component in mouse leukemias induced by Friend virus has been demonstrated by cytotoxic tests in vitro. Serum from mice of several inbred strains immunized with histoincompatible Friend leukemia tissue contained antibody that was cytotoxic in vitro for leukemia cells induced by Friend virus in the strains providing the immune serum. Unexpectedly, a high proportion of mice from strains that are highly susceptible to leukemogenesis by Friend virus did not develop leukemia after immunization as adults with incompatible viable Friend leukemia cells or with large amounts of infective filtrate. Cytotoxic sera could therefore be prepared in mice of both resistant and susceptible strains. By direct cytotoxic tests, and also by absorption studies, the Friend and Rauscher viruses appeared to induce the same antigenic change in the spleen cells of infected animals. A similar antigen has not been found in a variety of normal and leukemia tissues, including leukemias induced by the Gross Passage A virus.

63-1354 AN EVALUATION OF THE CARCINOGENICITY OF SIMIAN VIRUS 40 IN MAN. (E.) Fraumeni, J. F., Jr. (NCI, Bethesda), F. Ederer and R. W. Miller. J.A.M.A. 185(9):713-718, 1963.

The capacity of SV40 to produce subclinical infection in man, and to cause transformations suggestive of neoplasia in human tissue cultures, has raised questions about its oncogenic potential in man. To evaluate this potentiality, study was made of U.S. cancer mortality rates for 1950-1959,

the years encompassing the initiation of mass Salk vaccination in 1955. A slight rise, of uncertain significance, occurred in leukemia mortality rates for two age-groups under 25 yr. If the rise was due to SV40, it should be accentuated by comparing groups similar in all respects except for the content of viable SV40 in the polio vaccine admin. to each. Examination of the history of the early Salk vaccination program showed that it was possible to study one age-group, children 6 to 8 yr. old, who were immunized in a narrow span of time, May-July, 1955, with identifiable vaccine lots whose SV40 content could be estimated from stored samples. A cohort analysis was then made over the yr. 1950-1959 using cancer mortality data for children who were 6 to 8 yr. of age in 1955, classified according to three dose categories of SV40. Comparison of the cancer mortality experience of these three groups revealed no differences in trends following 1955, so recent increases in leukemia mortality were not attributed to the simian virus. A carcinogenic effect of SV40 would have gone undetected in this study if the latent period was longer than 4 yr., if the relatively low dose of SV40 in the vaccine was insufficient to induce cancer, or if the vaccines were beyond the age of susceptibility.

63-1355 STUDIES ON LEUKEMOGENESIS BY CELL-FREE FILTRATES OF AKR MOUSE LEUKEMIA. (E.)

Okada, K. (Okayama U. Sch. Med., Japan), I. Miyoshi, N. Kawamura and M. Sato. Acta Haemat. Jap. 25(1):1-11, 1962.

Serial passage into isologous newborn mice of cell-free filtrates prepared from spontaneous AKR lymphatic leukemia resulted in the enhancement of the leukemogenicity of the filtrates; the agent has been carried through 4 cell-free passages. Frozen and thawed or lyophilized AKR leukemic tissues, and frozen cell-free leukemic filtrates, when inoc. into isologous newborn mice, accelerated the development of leukemia. During serial passages of the cell-free filtrates of spontaneous AKR lymphatic leukemia, transformations of the lymphatic leukemia to myelogenous leukemia, plasma cell leukemia and reticulum cell

neoplasm were observed. Homologous cell-free transmission of AKR lymphatic leukemia was successful in female AKR x male C3H/He/Misima/Kyoto F1 and male AKR x female C3H/He/Misima/Kyoto. In addition, the filtrates induced lymphatic leukemia in 33.3% of C3H(f) mice of the Baylor Medical College colony. The C3H(f) leukemia was transplantable to isologous and C3H/He/Misima mice but not the AKR line. To date leukemia has not been induced in C3H/He/Misima, DBA, C57 Black and SM mice.

63-1356 A COMPARISON OF POLYOMA, "K", AND KILHAM RAT VIRUSES WITH THE ELECTRON MICROSCOPE. (E.) Dalton, A. J. (NCI, Bethesda), L. Kilham and R. F. Zeigel. Virology 20(3): 391-398, 1963.

Cells infected with polyoma, "K", and Kilham rat virus (RV) embedded in methacrylate were studied with the electron microscope. Particles present in polyoma and "K" virus-infected cells appeared to be identical in size (approx. 35 mμ), shape, and primary site of formation (intranuclear), although the cell types involved were different. Cytoplasmic inclusion bodies containing numerous characteristic particles were observed in endothelial cells and macrophages of the lungs of "K" virus-infected mice and were similar to those reported by others for polyoma. Many stromal cells of the kidney of hamsters infected with RV were observed to contain numerous intranuclear particles approx. 13 mμ in diameter. These particles did not exhibit the close packing typical of polyoma and "K" virus. Cells with cytoplasmic inclusion bodies containing similar particles were identified as macrophages.

63-1357 EXPERIMENTS ON THE LONG-TERM PRESERVATION OF ROUS SARCOMA. (Ger.) Schmidt, F. (Dept. Exp. Oncol. Res., German Acad. Sci. Berlin, Potsdam-Rehbrücke, Germany). Acta Biol. Med. German 10(5-6):615-617, 1963.

Lyophilized Rous sarcoma material to which chicken embryo homogenates had been added, could be successfully transferred even after 8 yr. storage.

See also abstract nos.: 1217, 1222

EPIDEMIOLOGY AND BIOMETRY

63-1358 STUDIES ON INCIDENCE OF SKIN CANCER IN THE KARELIAN AUTONOMOUS SSR. (Rus.) Voinin, V. V. (Republican Oncol. Dispens., Petrozavodsk, Karelian Autonomous SSR). Vop. Vopr. Med. Biol. 9(7):85-90, 1963.

For the yr. 1958-60 the death rate (per 100,000) from skin cancer was 0.61 for males and 0.28 for females. Incidence of skin cancer (per 100,000) was 3.6 (males) and 7.6 (females); in urban areas rates were, resp., 2.6 and 6.8, while in rural areas they were 5.2 and 9.1. The incidence of precancerous lesions was, resp., 5.8 and 8.1, in urban, and 5.8 and 4.4, among rural populations. When the Karelian SSR and the Sofia District (Bulgaria) were compared, rates for men were, resp., 8.9 and 22.8; and for women 9.3 and 17.4. When the Russian and Karelian populations of the SSR were compared, rates were 5.3 and 13.1, resp., for women and 3.2 and 3.9, resp., for men. Maximum incidences among men were in the age groups 60-64 and 75-79; in women in the 70-74 yr. age group.

63-1359 UNUSUAL CANCER MORTALITY AMONG A GROUP OF UNDERGROUND METAL MINERS. (E.) Hagoner, J. K. (NCI, Bethesda), R. W. Miller, E. Lundin, Jr., J. F. Fraumeni, Jr. and M. E. H. New Eng. J. Med. 269(6):284-289, 1963.

Among 654 underground metal (not including uranium) miners who had completed 15 yr. of mining before January 1, 1937 and were alive as of that date, the expected and observed deaths from neoplasms were, resp.: digestive system, 7.4 and 24; respiratory system, 7.0 and 22; other neoplasms 11.8 and 18. Similar data for 105 miners who completed 15 yr. between January 1, 1937 and December 31, 1948 were: digestive system, 16.8 and 27; respiratory system, 9.1 and 25; other neoplasms, 11.8 and 19. The 3-fold excess of cancer of the respiratory tract could not be attributed to an effect of age, smoking, activity, urbanization, socioeconomic status, heredity, diagnostic accuracy or silicosis. It appears likely that the mines contained inhalants that singly or in combination are carcinogenic.

63-1360 MALIGNANCIES IN CHILDREN. (E.) Handy, V. H. (Albany Med. Coll., N.Y.). J. Dis. Child. 106(1):54-64, 1963.

A study of malignancies was made of children in New York State exclusive of New York City. Reported is incidence of morbidity and mortality (male and female) for cancers tabulated as to site and for 3 time periods: 1941-43, 1949-51 and 1958-60. These results indicate the incidence and mortality rates showed little variation from the time period to another or between the sexes for carcinoma of all sites in the groups as a whole (age 0-14); in both sexes the rates were

highest during the first five yr.; leukemia was the most common form of malignancy in children, and accounted for almost one-half of all fatalities, with the highest rates being in the 0-5 yr. age groups.

63-1361 LUNG CANCER AND PREVIOUS RESPIRATORY DISEASE. (E.) Brett, G. Z. Tubercle 44(2):285-289, 1963.

The mortality rate from lung cancer in 135 men over 40 who had had pneumonia during the 3-7 yr. of observation, was 2.2%, which was not significantly different from that of 751 men in similar age groups who did not get pneumonia (3.1%). Over 50% of both groups were followed-up for more than 5 yr. There were no significant differences between the component groups of the controls (pts. with calcified tuberculous foci, bronchiectasis, pulmonary fibrosis, and those with normal chest X-rays).

63-1362 THE ASSOCIATION OF THYROID CANCER AND PRIOR IRRADIATION IN INFANCY AND CHILDHOOD. (E.) Rose, R. G. (Dept. Med., U. Texas M. D. Anderson Hosp., Houston), J. E. Hartfield, M. P. Kelsey and E. J. Macdonald. J. Nucl. Med. 4(4):249-258, 1963.

Among 216/426 pts. with thyroid cancer seen at the U. of Texas M. D. Anderson Hospital and Tumor Institute from 1944 through 1961 who replied to questionnaires, 70 reported a positive history of previous irradiation. Included were 2/2 under age 10, 18/31 (58%) age 10-19, 20/47 (43%) age 20-29, 18/53 (34%) age 30-39, 7/32 (22%) age 40-49, 2/25 age 50-59, 1/17 age 60-69, 2/8 age 70-79, and 0/1 age 80-89. About 71% had received radiation therapy in the head and neck area, while approx. 20% received radiation to the chest area. Latent period in the group of 70 averaged 12 yr. (range 1-34, mode 10 yr.). The marked decrease in those irradiated in relation to age may reflect the fact that irradiation of the thymus of infants and of acne in adolescents and adults was introduced in the 1920's and 1930's so that adults in that period would rarely have been irradiated. When 175 were compared with an equal number of noncancer pts. matched for ethnic group, age, yr. of admission and geographic location, there was a significantly greater frequency of previous irradiation (46/175 compared to 10/175). Other related series are also reviewed (48 references).

63-1363 EPIDEMIOLOGY AND TREATMENT OF LUNG CANCER IN SEATTLE. (E.) Ravenholt, R. T. (Div. Foreign Quarantine, U.S. Public Health Serv., Paris) and W. H. Foegen. Dis. Chest 44(2):174-185, 1963.

Diagnosed lung cancer deaths/100,000 population (in Seattle-King County, Wash.) rose from 3.8 (women) and 4.7 (men) in 1935 to 4.3 and 36.8, resp., in 1960. Although no increase in the mortality rate has been noticed among men less than 50 during the last ten-yr., a significant rise has been noted in those men 50 and over. No significant change has been noted in female mortality rates during the past 25 years. Present differences cannot be entirely attributed to increase in the efficiency of diagnostic methods. In 99 of 152 pts. dying of cancer in 1955, the histologic types were identified as follows: 50% dermoid carcinoma, 25% undifferentiated, 20% adenocarcinomas and 5% alveolar-cell carcinomas. The authors suggest that if the present high incidence in lung cancer in men develops into a plateau, it would probably largely be the expression of the effects of cigarette smoking upon men born after 1900; if it represents a peak despite continued exposure to various agents, then one must conclude that a large portion of adult males is unusually susceptible to some previous unidentified precipitating factor, such as the 1918-1920 influenza pandemic.

- 63-1364 CONGENITAL ABNORMALITIES IN CHILDREN BORN IN ALBERTA DURING 1961: A SURVEY AND A HYPOTHESIS. (E.) Vann, L. J. (Provincial Training Sch., Red Deer, Alberta, Canada). Canad. Med. Assn. J. 89(3):120-126, 1963.

In Alberta province, neonatal congenital physical abnormalities increased from 7.9/1000 births in 1959 to 13.8 in 1961. There appeared to be no correlation to drugs taken by the mothers during pregnancy, including antiemetics and tranquilizers. There was a relationship between the amount of precipitation and the number of malformations. In Northern Alberta, where precipitation is highest, 15.5/1000 children born in 1961 showed physical defects; in Southern Alberta, where precipitation is lowest, 11.9/1000 malformed children were born. In recent yr. there have been increases of radioactive dust containing Ce^{137} , Cr^{144} and Sr^{90} associated with above-ground Soviet thermonuclear Arctic explosions. The hypothesis is advanced that children born in Alberta in 1962 will show a greater incidence of physical deformities than those born in 1961, owing to greater rainfall during 1961 and 1962.

- 63-1365 SARCOMAS IN AFRICA. (Fr.) Bernard, J. Nouv. Rev. Franc. Hemat. 3(2):101-104, 1963.

In an editorial article data relating the occurrence of the Burkitt type sarcoma to a viral agent are reviewed briefly, and the importance of these findings is emphasized.

- 63-1366 LEUKEMIA DEATH RATE IN NORWAY, 1927-1960. (Nor.) Bjelke, E. T. Norsk. Laegeforen 83(10):877-881, 1963.

The rise in the reported leukemia death rate in Norway, especially in the population over 50, is ascribed primarily to improved diagnosis and more widespread, effective medical care. For males in the 60-69 and 70+ age groups, the rate per 100,000 inhabitants has increased from 5.6 and 4.8, resp. in 1931-35, to 19.7 and 39.2 in 1956-60; for females in these same age groups, from 2.8 and 1.4, resp., in 1931-35, to 12.8 and 26.2 in 1956-60. In the 15-29-year-old group, which has the lowest rate of mortality from leukemia, there has been no statistically significant rise since the period 1945-49. Leukemia remains a relatively rare cause of death, accounting for only 0.8% of the total mortality in 1960, and 4.6% of the total deaths from malignant diseases. In both sexes, leukemia mortality is highest in Oslo, lower in provincial towns, and lowest in rural areas.

- 63-1367 THE ETIOLOGY OF CANCER OF THE STOMACH. (Nor.) Myhre, E. (Inkognitogt. 26, Oslo, Norway). T. Norsk. Laegeforen 83(10):871-876, 1963.

In a review of the pertinent literature (27 references), the author discusses the often suggestive, but still inconclusive, results of epidemiologic studies, clinical and pathoanatomic observations, and experimental investigations. While significant differences, presumably related to dietary habits, have been found in the incidence of gastric cancer in different countries and social strata, as well as suggestive sequence of precancerous gastric mucosal changes and subsequent development of malignancy, no general hypothesis has been formulated to account for the fact that this is the most widespread of all malignancies.

- 63-1368 THE INCIDENCE OF INDEPENDENT TUMORS AMONG UTERINE CANCER PATIENTS. (E.) Bailar, J. C., III (NCI, Bethesda). Cancer 16(7):842-853, 1963.

Of 5,366 pts. with cancer of the uterus (cervix, 3,008; corpus, 2,358) diagnosed between 1935-1951, 199 (3.7%) have developed a total of 205 subsequent independent non-uterine cancers. The incidence of reported tumors of various sites is compared with the incidence in the general population and related to the age of the pts., the histological type of the original uterine cancer, and the treatment given. There seems to be an excess of breast cancer among women who have had adenocarcinoma of the uterine corpus and of urinary bladder tumors among pts. with cervical cancer. The incidence of several other forms of cancer may also be high. Definitive study of this problem would require a larger series of cases.

1369 THE NATURAL HISTORY OF LUNG CANCER. (E., Abstract) Boucot, K. R., D. A. Cooper and W. Weiss. Am. Rev. Resp. Dis. 88(1):102, 1963.

As part of a prospective survey of pulmonary neoplasia in men over 45, it was found that among 137 surveyed semiannually by means of photoradiographs, prevalence of proved lung cancer at entry into the study was 11/1,000. Over a follow-up period of 6.5-10 yr., 63 new cases developed. The annual incidence rate over this period almost doubled to about 2/1,000. Previous roentgenographic abnormalities such as disseminated fibrosis or inactive tuberculosis were present in 33 of the 63 cases.

1370 OBSERVATIONS ON THE INCIDENCE, BIOLOGY, AND PATHOLOGY OF SKIN CANCER AMONG FILIPINOS. (E.) Pantangco, E. E. (Dept. Path., Santo Tomas, Manila, Philippines), M. Canlas, Basa and R. Sin. J. Philipp. Med. Assn. 4(4):259-270, 1963.

In 1960 cancer ranked 7th among the principal causes of death (2.3% of 212,688 registered deaths) in the Philippines. The incidence (percentage) of the 10 most common sites of cancer at the University of Santo Tomas Hospital (1953-59), North General Hospital (1946-1960) and Philippine General Hospital (1947-1956) were, respectively: uterus - 13.47, 32.2, 7.30; breast - 10.4, 10.5, 11.8; oral mucosa, palate and tongue - 1.86, 4.1, 16.41; skin - 8.9, 6.0, 5.4; reticuloendothelial, lymph nodes - 7.67, 3.4, 2.25; colon and anal canal - 6.6, 4.19, 4.85; stomach - 5.22, 0.08, 2.56; liver - 3.43, 0.91, 1.37; nasopharynx - 1.35, 1.12, 0.64; and ovary - 2.84, 4.98, 1.80. Among a total of 330 cases of skin cancer, incidence in relation to age was: 31-40, 11.87%; 41-50, 24.54%; 51-60, 23.33%; 61-70, 17.57%; over 70, 11.82%. The number of cases and male/female ratios (percentage values) were: epidermoid cancer - 180 cases, 57.2/42.8; basal cell - 104 cases, 38.5/61.5; melanoma - 41 cases, 70.7/29.3; adnexal - 5 cases, 40/60. Epidermoid cancers were found primarily in the head and neck (121 cases). Of 104 basal cell carcinomas, 92% were of the nodular type, nasolabial folds, eyelids, forehead and ears; 8% of malignant melanomas were in the lower extremities, especially the foot. Of adnexal cancers, 3 were of the forehead and scalp. In the series of 330 skin cancer cases, 67% were found in the exposed areas of the head, neck and lower extremities; women had as high an incidence of skin cancer as men and are equally exposed to the same solar factors in the rice fields and on the river banks, where most laundry women do their washing. Repeated trauma and irritation was considered a definite factor in 15 cases of malignant melanoma. Squamous carcinomas developed in 3 pts. whose feet were irradiated for athlete's foot 10-15 yr. previously. No cases appeared to be associated with faulty diet, industrial chemicals, or factors associated with smoking.

63-1371 FOLLICULAR MAXILLARY CYSTS, BASAL CELL TUMORS, AND BONE ANOMALIES AS PARTS OF A HEREDITARY SYNDROME. (Dan.) Rasmussen, E. Nord. Med. 69(21):606-612, 1963.

Personal observations on this syndrome are reported which covers 40 individuals belonging to 4 families and which includes 11 pts. (5 female and 6 male, aged 6-55) each with 2 or more of the component conditions. In family A (14 members in 3 generations) 5/9 members who were studied were affected. All had basal cell tumors, all but 1 had maxillary cysts, and 1/5 had a costal deformity. One 18-year-old boy in this family also had a syringoma of the back, which was undergoing transition to a cylindroma. In family B (19 members in 3 generations) 5/10 members who were studied were affected. All 5 had basal cell tumors, 4/5 had maxillary cysts, 3/5 had costal deformities, 2/5 had fused vertebrae (and spina bifida), and 1/5 had all four stigmata, as well as Sprengel's deformity. Only one affected member each could be found in families C and D. Except for vertebral fusion, not present in one of them, both pts. had all 4 characteristic anomalies. In all 11 cases, the skin tumors were classifiable as epidermal adnexal tumors; and the most frequent histologic diagnosis was basal cell adenoma. These findings are compared with those in similar cases reported in the literature (34 references).

63-1372 PRIMARY AND METASTATIC BONE TUMORS. (Pol.) Dubinska, A. (Dept. Orthopedic Surg., Acad. Med., Warsaw, Poland) and Z. Piskorska. Chir. Narzad. Ruchu Ortop. Pol. 28(2):209-218, 1963.

Analysis of the records of 11,546 pts. treated for trauma over a 10-year-period revealed 110 cases of bone tumor, an incidence of 0.95%. Of these, 46 (42%) were primary tumors (36 benign and 10 malignant), and 31 (28%) were metastatic; the other 33 (30%) were classified as pseudotumorous lesions. In 40% of the cases the pts. themselves were convinced that the trauma was responsible for the tumor, which was discovered from 3 mo.-10 yr. after the injury. Of the 10 malignant primary tumors, 5 were osteosarcomas, 2 were neurosarcomas, and there was 1 each of plasmocytoma, plasmocellular carcinoma, and synovial sarcoma. Pathologic fractures occurred in 4 of the 10. Three illustrative cases are detailed in which the traumatic origin of the bone tumor seemed particularly obvious. All 3 pts. were young (17, 12 and 18 yr., resp.), and in the first 2 cases the post-traumatic tumors were malignant: one a fatal neurosarcoma, the other a synovial sarcoma removed by amputation of the affected finger and the first metatarsal bone.

63-1373 MORTALITY FROM LEUKEMIA IN POLAND IN THE YEARS 1950-1959 WITH CONSIDERATION OF CERTAIN PROBLEMS OF EPIDEMIOLOGY. (Pol.) Rattka, P. (Inst. Oncol., Gliwice, Poland).

Nowotwory 13(1):61-74, 1963.

Polish mortality statistics for the 10-yr. period surveyed show a sharp increase (163%) in deaths from leukemia (from 1.4/100,000 in 1950 to 3.2 in 1959), especially in rural areas, although the actual mortality from this disease is higher in towns and cities. There is no direct correlation between level of industrialization and mortality from leukemia or the rate of its increase.

Mortality was higher among males: in 1950, the rates for males and females (per 100,000) were 1.8 and 1.0, resp.; in 1959 this sex difference was somewhat narrowed to 3.5 and 2.8, resp. The mortality from leukemia was greatest in those over 50 yr. of age and has risen in recent yr.: incidences in age groups 55-64 and 65-74 were 2.8 and 3.9, resp., in 1950 and rose to 7.1 and 9.7, resp., in 1959. Lymphocytic leukemia is the predominant form in Poland, with the highest incidence in the older age groups up to age 70, after which it declines sharply. Mortality from malignant tumors has not risen as sharply as the leukemia mortality, although in 1958, leukemia still accounted for only 3.8% of the total mortality from malignant disease. These statistics are believed to reflect an actual increase and not just improved diagnosis and reporting. In discussing the possible reasons for the increase, the author states that in 98.8% of the 143 cases of leukemia seen at his own institute, there was nothing in the history to suggest that exposure to noxious agents or ionizing radiation was an etiologic factor. Leukemia mortality in Poland, though rising, is still far below that in other countries of Europe and the USA.

63-1374 SOME THERAPEUTIC PROBLEMS IN MALIGNANT DISEASES OF THE LYMPHORETICULAR SYSTEM. (Pol.) Wiczorkiewicz, A. (Inst. Oncol., Gliwice, Poland), K. Schneiberg and B. Zaremba. Pol. Tyg. Lek. 18(22):789-792, 1963.

The observation of 3 cases of lymphogenic neoplasia with ultimate leukemia led the authors to reexamine the relationship between leukemia and malignant tumors. The first pt. was a 42-year-old woman with lymph node enlargement for 3 mo., identified at biopsy as a malignant lymphogenic tumor (lymphosarcoma?). On admission, she had slight leukopenia, but after X-ray treatment (3750 r in 3 wk.), the WBC count rose to 25,700 and the pt. died 10 days after the end of treatment. The other 2 pts. were 4-year-old children--a boy and a girl--with enlarged lymph nodes histologically diagnosed as lymphosarcoma and probable lymphosarcoma, resp. In both cases the symptoms had been present for 4 mo. The first child had a WBC count of 11,300 on admission, the second, a count of only 2800. Both were given X-ray treatment. In the first case, the lymph node enlargement regressed temporarily, but the WBC count later rose to 12,000. Treatment with cytostatic agents was unsuccessful; lymph

nodes became enlarged and WBC, after transient reduction, rose to 10,300, with 22% blast cells. The second child, discharged in a good condition after responding well to X-ray treatment, relapsed after 1 mo.; WBC count was 154,000, all of the blast cell type. After treatment with cytostatics she showed no improvement and was discharged in very poor condition and was lost to follow-up. Although many authors believe that there is no clear demarcation between lymphoreticular neoplasia and lymphoreticular leukemia, X-ray treatment is suspected of triggering the terminal leukemic phase in all 3 of these cases.

63-1375 A STATISTICAL SURVEY OF NEOPLASMS AMONG KOREANS. A SECOND REPORT. (E.)

Dong Sik Kim (Yonsei U. Coll. Med., Seoul, Korea), Soon Eung Kim Byung Ho Choi and Jac Eun Bahng. Yonsei Med. J. 3:51-59, 1962.

When 7,778 surgical and autopsy specimens, collected in the 52 mo. prior to August 1961, were examined as part of a continuing study, 1,587 neoplasms were found: 480 benign and 1,107 malignant. The most frequent carcinomas in the male were those of the stomach (83 cases, mostly adenocarcinomas, av. age 47.6 yr.), lymph node (56, metastatic), pharyngo-larynx (40), skin (36), liver (30), intestine (24), rectum (23), nasal cavity (22), omentum (18), and lung (16); in the female, those of the uterus (265, mostly squamous-cell type, av. age 45.2 yr.), mammary gland (48, mostly adenocarcinomas), stomach (27), ovary (20), vulva (19), lymph node (18), rectum (17), nasal cavity (15), skin (15), and thyroid (14). Incidence (percentage for males and females in relation to age was, resp. 31-40, 14.4 and 23.3; 41-50, 28.3 and 32.9; 51-60, 32.5 and 22.6.

63-1376 MEDICINAL ARSENIC POISONING AND LUNG CANCER. (E.) Robson, A. O. (Roy. Victoria Infirm., Newcastle, England) and A. M. Jelliffe. Brit. Med. J. 1:207-209, 1963.

Six previously unreported cases are presented (four female and two male) which may indicate a causal relationship between the therapeutic admin. of inorganic arsenic and later development of bronchial carcinoma. Arsenic was prescribed for psoriasis, rheumatic fever, convulsions, or as a general tonic. The av. latent period before the clinical onset of lung cancer was 32 yr., and all the tumors were poorly differentiated carcinomas. All pts. had skin manifestations of chronic ingestion of arsenic. Only two of them had ever smoked cigarettes.

63-1377 COMPARATIVE INCIDENCES OF MALIGNANCIES IN VILNO AND FRUNZE DURING 1959. (Rus.) Stukonis, M. K. (Lithuanian Inst. Oncol., Vilnius, Lith. SSR) and R. G. Nikitina. Vop. Onkol. 9(5): 95-99, 1963.

ing 1959 there were 399 malignancies in Vilno and 472 in Frunze (FR), to give incidences (per 10,000) of 16.9 and 21.1, resp. Male pts. numbered 164/399 and 213/472, resp., or incidences (per 10,000 of male population) of 15.6 and 21.0. Males included 235/399 and 259/472, resp., or incidences of 18.0 and 21.1. Localization of malignancies (per 10,000) was, resp., for V, FR, and women V, FR: stomach - 5.4, 8.8; 3.4, 5.1; skin - 1.5, 1.6 and 2.4, 4.3; trachea - 2.7, 4.1; lung - 2.7, 2.7 and 0.7, 0.5; thyroid gland (women) - 2.8, 2.3; esophagus - 0.8 and 0.2, 0.7; lip - 0.6, 2.0 and 0.2, 0.3; rectum - 0.3, 0.2 and 0.3, 0.6; larynx - 0.9 and 0, 0; oral cavity - 0.1, 0.4 and 0.0. While some differences in morbidity rates between Vilno and Frunze can be attributed to their geographical locations, environmental conditions and food, elucidation of others will require further investigation.

1378 THREE SEPARATE CONCURRENT GYNECOLOGIC MALIGNANT NEOPLASMS IN ONE PATIENT.

(E.) Lee, R. A. (Mayo Clin., Rochester, Minn.), S. Welch and M. B. Dockerty. Am. J. Obstet. Gynec. 86(7):957-960, 1963.

The authors report the finding of the second case noted in the English literature of 3 separate concurrent primary malignant lesions of the genital system. The pt. was a white female, 60. At time of surgery, one of the tumors was found to have metastasized to the lungs. Grade II adenocarcinoma lined the entire endometrial cavity and endocervical canal; a Grade I leiomyosarcoma of the uterus had invaded the entire posterior uterine wall; and an intracystic Grade I papillary mucus cystadenocarcinoma was present in the right ovary. The uterus, both fallopian tubes, and ovaries were removed and a thoracotomy was performed.

1379 NEW FACTORS IN THE EPIDEMIOLOGY OF CANCER IN ANIMALS OF ECONOMIC IMPORTANCE. (E.) Campbell, J. G. (Agric. Res. Council, Poultry Res. Ctr., Edinburgh, Scotland). Acta Un. Int. Cancr. 19(3-4):652-654, 1963.

The introduction of hyper-intensive systems of rearing and feeding strains of baby chicks and other animals of economic importance, selected for rapid growth and early maturity, has produced a new problem in the epidemiology of cancer. In the case of "broiler" chickens, 76 tumors have been collected and examined, many of which are embryonal type tumors, occurring within a few wk. of hatching. Such tumors were previously rare. A similar phenomenon occurs in other hatcheries. The cumulative effect of artificial selection, food additives, high energy diets and environment is briefly discussed.

63-1380 AN EPIDEMIOLOGICAL STUDY OF OCCUPATIONAL BLADDER CANCER. (E.) Lieben, J. (107 Hillcrest Road, Camp Hill, Pa.). Acta Un. Int. Cancr. 19(3-4):749-750, 1963.

Recently a small chemical plant in Pennsylvania was found manufacturing β -naphthylamine. Some of the product was sold to a neighboring dye plant. Both plants denied the knowledge of occurrences of bladder cancer and a search for increased incidence of bladder cancer in death certificates revealed no increase. Hospital records of all admissions for bladder cancer from seven hospitals were analyzed. Their occupational histories were obtained and eleven cases who had worked in the plants concerned were identified. In regard to age, 3/11 were over 60 yr., 8 were under 60 yr. Among 67 bladder cancer cases in the general population, only 18 were under 60 and 49 were over 60. On further investigation of work records, it was learned 5/11 had definitely been exposed to β -naphthylamine; 4 others had been employed as general laborers, carpenters, and maintenance men; 2 according to management, had no direct contact with the product.

63-1381 CANCEROGENIC SUBSTANCES IN THE AIR OF CITIES AND POSSIBLE PREVENTIVE MEASURES. (E.) Gourinoff, B. P. (Erisman Res. Inst. Hygiene, Moscow). Acta Un. Int. Cancr. 19(3-4):737-738, 1963.

Because of the possible carcinogen content of various exhausts from motors, industrial plants and heating systems, methods are discussed which would lead to a reduction in these substances. Various heating systems were investigated, carburetor and diesel motors were also compared. The soot from carburetor motor exhausts was found to be carcinogenic while that of diesel engines was not. Use of coal tars for road pavements is prohibited in the USSR.

63-1382 THE COMPLEX AETIOLOGY OF LUNG CANCER. (E.) Dean, G. (Provincial Hosp., Port Elizabeth, S. Africa). Acta Un. Int. Cancr. 19(3-4):721-723, 1963.

The incidence of lung cancer in S. Africa, Australia, New Zealand and the U.S. is half, or less than half, the incidence in Britain. Cigarette consumption has long been higher among white S. Africans, and as high in the U.S., Australia and New Zealand, as in Britain. British immigrants to S. Africa, Australia, New Zealand and the U.S. have a higher lung cancer incidence than the native born, but a lower incidence than those who stayed in Britain. Apparently the British immigrant carries with him an increased risk that is not related to cigarette smoking. Lung cancer rates are higher in urban than in rural areas; in rural S. Africa moderate cigarette smoking causes little increase in the

lung cancer risk, although particularly in the cities, lung cancer incidence is higher among cigarette smokers than non-smokers. There would appear to be a synergistic effect between the environmental air and tobacco smoke in its effect on the bronchial cells.

- 63-1383 CIGARETTES, ARSENIC AND LUNG CANCER. (E.) Buechley, R. W. (Sch. Public Health, U. California, Los Angeles). *Acta Un. Int. Cancr.* 19(3-4):718-720, 1963.

Certain non-smokers show very high lung cancer mortality: miners at Schneeberg and smelter workers at Aue, Saxony; dwellers near copper mines and smelters in Montana; and vineyardists in the Rhineland. A known carcinogen common to all these disparate environments is arsenic: nickel arsenides at Schneeberg and Aue, enargite at Butte, lead arsenate sprays in vineyards. The lead arsenate content of cigarette tobaccos has reached over 50 ppm, fifteen times the allowable residue on foods, thus incriminating arsenic in the world-wide epidemic of smokers' cancer. This epidemiological chain obviates explanations based on radioactivity. It requires further investigation of arsenic-exposed populations, and, as a counterpoint, investigation of lung cancer among smokers of unsprayed tobacco or of tobacco sprayed with other insecticides.

- 63-1384 DEVELOPMENT OF FLEXNER-WINTERSTEINER ROSETTES IN RETINOBLASTOMA OF JAPANESE PATIENTS COMPARED WITH THAT OF AMERICAN PATIENTS. (Jap.) Tsukahara, I. (Dept. Ophthal., Fac. Med. Kyoto U., Japan) *Ganka Rinsho* 16(12):1233-1235, 1963.

In a study of 30 eyes (from 29 pts.) exhibiting retinoblastoma, 3 types were recognized: well differentiated (rosettes over one-half of the area); less differentiated (or pure retinoblastoma, with only a few or no rosettes in tumor); and mixed (rosettes not predominant or occupied less than one-half of the area of the tumor). The incidences of the 3 types were, resp., 2, 24, and 4. In a previously published American series of 150 eyes, incidences were, resp., 51, 74 and 25, indicating a relatively lower incidence of the well differentiated type in the Japanese series.

- 63-1385 CONTRIBUTION TO THE STUDY OF MULTIPLE TUMORS: TRIPLE PHARYNGEAL-LARYNGEAL CARCINOMA FOCI. (It.) Aragno, F. (Inst. Clin. Otorhinolaryn., U. Turin, Italy) and A. Sartoris. *Cancro* 15(6):750-765, 1962.

A case of three carcinomas in a single pt. is presented. The first was on the right vocal cord, the second in the region of the right velum palatinum and the third on the left false cord. The second and third tumors appeared 6

and 8 yr., resp., after the first. Associated epithelial changes consisted of hyperplasia, dyskeratosis, acanthosis and carcinoma *in situ*. The 3 tumors developed slowly, perhaps due to an immunological reaction established in the organ by the first tumor or by the early dysplastic processes. It is suggested that all 3 tumors were probably related to a single histopathogenic factor arising in a constitutional disturbance of the reactivity of the mucosae of the upper respiratory and digestive passages, resulting in a dyskeratotic and neoplastic reaction to stimuli which were not in themselves carcinogenic.

- 63-1386 TUMORS OF THE CENTRAL NERVOUS SYSTEM. INDUSTRIAL CONSIDERATIONS. (E.) Mancuso, T. F. (1450 Arlington Ave., Columbus, Ohio). *Acta Un. Int. Cancr.* 19(3-4):488-489, 1963.

The study of cancer death in 1947 in Ohio disclosed an unusual incidence of central nervous system tumors. The finding was substantiated by analysis of deaths over longer periods and especially in former workers in the rubber industry. The increase in CNS tumors was located essentially in Summit county, center of the rubber industry. An urban excess and excess of male over female cases was established. The presumption is that the rubber industry may be responsible for this particular tumor incidence.

- 63-1387 THE DETERMINATION OF 3,4-BENZOPYRENE IN THE ATMOSPHERE OF PRAGUE. (E.) Skramovsky, V. (2nd Dept. Biochem., Charles U., Praha, Czech.). *Acta Un. Int. Cancr.* 19(3-4):733-736, 1963.

From the 3,4-benzpyrene (BP) conc. measured in town atmosphere by an aspiration technic, it is to be concluded that the chief source of BP in Prague are dwelling house heating installations. Average monthly conc. during the heating season (October to March) was 4.6-12.2 $\mu\text{g}/100 \text{ meter}^3$; during the summer season (April to September) av. monthly conc. of BP was 1.3-3.6 $\mu\text{g}/100 \text{ meter}^3$. In one industrial zone av. and max. conc. during the heating season was 2.1 and 2.2, resp.; av. and max. conc. for 2 industrial zones during the summer season were 0.8 and 1.2 for one and 1.5 and 2.3 for the second.

- 63-1388 THE ROLE OF 3:4-BENZOPYRENE IN THE EPIDEMIOLOGY OF LUNG CANCER. (E.) Waller, R. E. (St. Bartholomew's Hosp., London, E.C. 1). *Acta Un. Int. Cancr.* 19(3-4):486-487, 1963.

The great increase in lung cancer which has taken place during the past 30 yr. cannot be directly connected with changes in the 3,4-benzpyrene (BP) content of the air, for in British towns there has been a tendency for the conc. to decline during the same period. Earliest measurements of BP in London were made in 1948 and the conc. of

smoke can be used as a guide to earlier conditions. The difference in lung cancer mortality between urban and rural areas, and between towns in different parts of the country could be linked with the conc. of BP, but here there are difficulties. The present trend in Great Britain is for the conc. of smoke to decline more rapidly in the larger than in the smaller towns, and in recent yr. there has been a smoothing out of smoke conc. to a more uniform level. Lung cancer mortality is also becoming more uniform within Great Britain, but it would be difficult to associate these 2 findings with certainty.

1389 MORBIDITY AND MORTALITY IN MAN CAUSED BY PULMONARY CANCER AND ITS RELATION TO THE POLLUTION OF THE ATMOSPHERE IN THE AREAS AROUND ALUMINUM PLANTS. (E.) Litvinov, N. N. (N. Sysin Inst. Gen. Public Hygiene, Acad. Med. USSR, Moscow), M. S. Goldberg and S. N. Mina. Acta Un. Int. Cancr. 19(3-4):742-745, 1963.

A study of the discharge of carcinogens from aluminum plants by sedimentation and aspiration methods, it has been calculated that they discharge into the air each day over 10 kg of 3,4-benzopyrene (BP). There appears to be greater discharge of BP from aluminum plants than from other industrial plants; such discharge was detectable up to a distance of 7 kilometers. In a study of chronic morbidity of the respiratory tract in 3 groups, a positive correlation with air pollution was established, as was done for lung cancer incidence.

1390 SQUAMOUS-CELL CARCINOMA ASSOCIATED WITH A DENTIGEROUS CYST OF THE MANDIBLE. (E.) Williams, I. E. (VA Hosp., Memphis, Tenn.) and C. W. Newman. Oral Surg. 18(8):1012-1016, 1963.

Plastic changes within simple odontogenic cysts appear to be a rare but definite entity. A review of current American and foreign literature reveals several well-documented cases. A case is described of a 59-year-old man with a radio-opaque area in the region of missing maxillary central and lateral incisors. Questioning revealed a history of pain 6 mo. previously. On surgical exploration a cystic-appearing soft-tissue mass was seen which was diagnosed as a squamous cell carcinoma of the well-differentiated type.

1391 ARSENIC AND VISCERAL CANCER. (E.) Russell, B. F. (London Hosp., Whitechapel, E.1, England). Brit. Med. J. 1:503, 1963.

In relation to the suggested causal relationship between inorganic arsenic and later development of bronchial carcinoma, 320 pts. with epithelial neoplasms on the exposed parts of the body and no

history of arsenic were compared with 11 pts. with a certain or probable history of earlier ingestion of inorganic arsenic. In the non-exposed group 306 had no visceral malignancy and 14 (4.4%) had visceral malignancy, of whom 7 (2.2%) had bronchial malignancy (1 in the breast also). In the exposed group 5 had no systemic malignancy, 5 (45.5%) had bronchial malignancy and 1 had carcinoma of the vulva. The data indicate the desirability of pooling information about pts. who were treated with inorganic arsenic many yr. ago.

63-1392 EPIDEMIOLOGICAL CONSEQUENCES OF AN ARSENIC-LUNG CANCER THEORY. (E.) Buechley, R. W. (Sch. Public Health, U. California, Los Angeles). Am. J. Public Health 53(8):1229-1232, 1963.

Essentially the same material presented in CRA 1(7):#1383, 1963. (See also CRA 1(7):#1376, 1963.)

63-1393 THE IMPORTANCE OF TRAUMATIZATION OF THE PIGMENTED NEVI. (Cz.) Trapl, J. (Dept. Gen. Med., Charles U., Prague) and L. Paleček. Cesk. Derm. 38(3):169-173, 1963.

From a study of his own material as well as data reported in the literature, the authors feel the importance of injury to pigmented nevi has been overestimated. Most reports deal with injuries to an already existing tumorous process, and not to quiescent junctional nevi. From the total number of 220 cases of melanoblastoma examined by the authors, traumatization could be proved in 43 pts., i.e. 32%, where the tumor was preceded by a nevus. In 36 of these pts., i.e. in 27%, the trauma was inflicted on an established malignant tumor; only in seven, i.e. 5%, was there development of a tumor after injury of a junctional nevus. On the other hand in keeping with data reported in the literature, the authors draw attention to the possible role of trauma as a potential provoking factor in the development of melanoblastoma of the skin, where previously no nevus could be detected. This was found to be the case mostly in tumors on the plantar surface of the foot (seven cases) or under the nail (four cases).

63-1394 THE RELATIONSHIP OF THE USE OF TOBACCO AND ALCOHOL TO CANCER OF THE ORAL CAVITY, PHARYNX OR LARYNX. (E.) Vincent, R. G. (Roswell Park Mem. Inst., Buffalo, N.Y.) and F. Marchetta. Am. J. Surg. 106(3):501-505, 1963.

When 106 pts. with carcinoma of the oral cavity, pharynx or larynx were interviewed, a history of heavy consumption of alcohol was given by 62% of the pts., and 85% smoked the equivalent of one or more packs of cigarettes a day. The male:female ratio was 5.2:1; mean age of diagnosis for the entire series was 62 yr. Of all the pts. with oral carcinoma in this study, a second primary

malignant lesion developed in 7.5%. Although the etiologic mechanism is not understood, additional supporting evidence indicates that the habitual use of tobacco and alcohol plays an important role in the cause of oral carcinoma.

- 63-1395 STATISTICAL INVESTIGATION OF ACUTE LEUKEMIA. (It.) Introzzi, P. (Inst. Clin. Med., U. Pavia, Italy), E. G. Rondanelli, P. Gorini, and G. Casirolo. *Haematologica* 68(1): 1-28, 1963.

Among 55,746 pts. seen at Pavia's Medical Clinic from 1941 to the end of the first semester of 1962, there were 482 cases of leukemia (0.864%). Incidence of acute leukemia was 0.437%, that of the chronic forms 0.434%. During the period of study there was a marked increase in frequency of the acute forms. Highest incidence of acute leukemia in relation to age occurred in infancy; in subsequent periods there was observed an irregularly decreasing incidence with a tendency to stabilize in the older age groups. Conversely the incidence of chronic leukemias increases with increase in age. Males are affected more than females, with a greater difference in regard to chronic leukemia. In acute leukemias the different incidence between both sexes has had a tendency to decrease during the last yr. of observation, namely the incidence rate tends to be the same. This observation could be explained by assuming a factor or a number of causal exogenous factors, which, in the last few yr., have equally affected both sexes. Among possible leukemia-inducing exogenous factors a paramount role has been ascribed to ionizing radiations, whose influence on the incidence of acute leukemias has been emphasized.

- 63-1396 ENDOCRINE ADENOMATOSIS AND PEPTIC ULCER IN A LARGE KINDRED. INHERITED MULTIPLE TUMORS AND MOSAIC PLEIOTROPISM IN MAN. (E.) Wermer, P. (Dept. Med., Presbyterian Hosp., New York). *Am. J. Med.* 35(2):205-212, 1963.

An ancestral line, consisting when originally recorded in 1954 of five pts. affected by the syndrome of adenomatosis of endocrine glands and peptic ulcer, now includes 15 other members of the family also affected by the disease; 19/20 pts. suffered from peptic ulceration. The pattern of peptic ulcer and tumors of the anterior pituitary gland, parathyroid glands and islets of Langerhans must now be augmented to include adenomas of the thyroid and of the adrenal cortex, as well as lipomas in various locations. It is proposed that the genetic mechanism in the pathogenesis of the syndrome is that of 'mosaic pleiotropism'. The very multiplicity of tumors in the affected endocrine glands is a consequence of their genetic character.

- 63-1397 THE QUESTION OF AN INTERDEPENDENCE BETWEEN TONSILS AND CARCINOMA OF THE UPPER AIR AND DIGESTIVE PASSAGES. (Ger.) Matzker, J. (Ears, Nose, Throat Clin., Johannes Gutenberg-U., Germany) and P. Schmidt. *Zschr. Laryng. Rhinol. Otol.* 42(5):363-371, 1963.

After examination of 5000 normal controls and 542 pts. with carcinomata of the upper air and digestive passages, earlier findings were confirmed showing that there was a distinctly smaller number subjected to tonsillectomy in the carcinoma group as compared with the rest of the population unaffected by tumor. These differences are statistically significant. With regard to the possible relationship between the tonsils and the origin of carcinoma, it is suggested that other clinics should also undertake suitable investigations.

- 63-1398 EFFECTS OF SUNLIGHT ON THE INCIDENCE OF CARCINOMAS AND MALIGNANT MELANOMAS IN THE TROPICAL AND SUBTROPICAL AREAS OF AUSTRALIA. (E.) Belisario, J. C. *Derm. Trop.* 1(3):127-136, 1962.

The incidence of skin cancer in Australia is the highest in the world. Heredity plays an indirect but important role in that it provides a suitable pabulum (a fair skin) for the growth of cancer. Statistics from various parts of the world show the importance of pigment in dark-skinned individuals as a protective factor against the carcinogenic radiations of the UV component of sunlight, especially wavelengths between 2,900 and 3,341 Å for humans. The protective effect of lipstick accounts, at least in part, for the lower incidence of lip cancer in women. The habits of outdoor work and sport, with large areas of the body uncovered, account for the generally higher incidence of skin cancer in men than in women. Approx. 90% of skin cancer occurs on exposed areas. The number of sunshine hr. is more important etiologically than the degree of intensity of exposure. Among other possible or probable factors of etiologic significance are the amount of water vapor and ozone in the atmosphere; altitude above sea level; variations in solar distance from the sun (seasons); zenith distance of the sun (time of day); and various applications of substances on the skin and prolonged and repeated local irritation or trauma.

- 63-1399 THE EPIDEMIOLOGY OF LIP, ORAL, AND PHARYNGEAL CANCERS, AND THE ASSOCIATION WITH SELECTED SYSTEMIC DISEASES. (E.) Keller, A. Z. (Public Health Res. Inst., New York). *Am. J. Public Health* 53(8):1214-1228, 1963.

A sample of 2,177 males with cancer of the lip, oral cavity or pharynx, discharged in a 5-yr. period from VA hospitals is compared with control

ts. having bronchitis and emphysema or rheumatoid arthritis, and with the living population of veterans, the total discharges from these hospitals, the rates of hospitalization, and the US population of white males. Except for cancer of the lip, which occurred more frequently in the South, the geographical distribution of cancer cases was generally similar to that of the controls. It also appeared that apart from lip cancer, which was extremely rare in Negroes, other oral cancers were not selective for race. Cancer of the salivary glands had a considerably younger age distribution than that of other oral cancers. Cancer of the upper lip was less frequent than that of the lower lip, and also occurred at an older age. No association was found between the cancers and diabetes mellitus, generalized arteriosclerosis, chronic alcoholism, and syphilis. A marked association between cancer of the floor of the mouth and cirrhosis of the liver was seen. It has not been possible to explain this association on the basis of bias or artifacts of the data; it appears to be a genuine association.

-1400 THE PRESENTATION OF MALIGNANT MELANOMA (MELANOBLASTOMA). (E.) Milton, G. W. (Dept. Surg., U. Sydney, Australia) and C. W. D. Lewis. S. Afr. Cancer Bull. 7(2):63-70, 1963.

e CRA 1(2):#302, 1963.

-1401 MALIGNANT NEOPLASMS AS CAUSE OF DEATH IN THE CZECHOSLOVAK SOCIALISTIC REPUBLIC DURING THE LAST DECADE. (E.) Wunder, R. (Incol. Res. Inst., Bratislava, CSSR), J. Liska and P. Doval. Neoplasma 10(3):309-320, 1963.

e analysis of mortality attributed to malignant neoplasms in the Czechoslovak Socialist Republic is presented for the period 1949-1959 and includes overall incidence as well as according to site, age, and sex. In contrast to the trend up to 1948, mortality among males was found to be higher than among females. The most important site involved is the g.i. tract both in

males and in females, the urogenital system in females and the respiratory system in males. The evolutionary trend in the g.i. tract is stabilized, rate of increase in cancer of the breast and female genital organs is moderate, while cancer of the respiratory system in males continues to increase at a more rapid rate. A remarkable rise has been noted in mortality attributed to malignant neoplasms of the lymphatic and hematopoietic tissues in both sexes. Mortality from cancer of the urogenital system has been found higher in the older age groups of males than of females.

63-1402 MALIGNANT NEURINOMA. (Ger.) Behrendt, W. (Inst. Path., Karl Marx-U., Leipzig, Germany) and S. Schultrich. Zschr. Krebsforsch. 65(5):524-528, 1963.

When 53 neurinomata were studied histologically and examined regarding their biological behavior, they fell into 3 groups: benign (40); proliferating (12); and malignant (1). Follow-up studies of pts. in the latter 2 groups were made and the transition into a malignant neurinoma in one instance could be shown. Malignant transformation of neurinoma presumably occurs more frequently than previously supposed.

63-1403 CANCER OF THE LUNG INCIDENCE IN A MAJOR INDUSTRIAL CENTRE. (E.) Fershtudt, V. I. (Dept. Public Health Admin., 1st Moscow Med. Inst.). Acta Un. Int. Cancr. 19(3-4):746-748, 1963.

The lung cancer incidence in an entire industrial (unnamed) town and in smaller areas within the town revealed several "foci" of high incidence. In one such area a group of houses was situated within 500 meters of a chemical plant. Here the mortality rate for all malignant growths was 2-3x higher than the av. for the district and the town as a whole. Of those who lived in the area, 56% had been employed at the plant throughout their careers. Preliminary data indicate that most of them were subjected to the combined influence of harmful substances at work and at home.

See also abstract nos.: 1218, 1227

MISCELLANEOUS

63-1404 THE EFFECT OF HYPOTHALAMIC STIMULATION ON THE GROWTH OF TRANSPLANTED SARCOMAS.

(E.) Ukolova, M. A. (Rostov Sci. Res. Inst. Roentgenol., Radiol., Oncol., Min. Health RSFSR), Y. N. Bordyushkov and L. K. Garkavi. Biull. Eksp. Biol. Med. (Eng.) 53(5):588-591, 1963.

After electric stimulation of the hypothalamus (40 sec. 3x a day at 5-7 min. intervals, every 1-2 days) of male albino rats 1.5 mo. prior to and continued for 1 mo. after the transplantation of M-1 sarcoma, tumor suppression and often absorption was observed; whereas electric stimulation for less than 1 mo. after transplantation, only significantly intensified tumor growth. Cortical stimulation 3 wk. before and 9 mo. after transplantation with electrodes or spheres caused both tumor suppression and intensification, while hypothalamic stimulation with electrodes or spheres caused only tumor reduction. Similar results were obtained with Sarcoma 45 when hosts were stimulated before and after transplantation.

63-1405 SPONTANEOUS AND INDUCED CHANGES IN THE BIOLOGY AND GROWTH OF TUMORS. (Ger.)

Wrba, H. (Inst. Path., Ludwig-Maximilians U. Munich, Germany) and H. Rabes. Zschr. Krebsforsch. 65(4):316-324, 1963.

A discussion of spontaneous changes observed during an 8-year-period with the following experimental tumors: Walker carcinoma of the rat (solid and ascitic forms), also carried in mice and golden hamsters; Yoshida carcinoma (solid and ascitic forms) carried in rats and mice; and Zajdela Ascites Hepatoma of the rat (in rats and golden hamsters); finally, Ehrlich ascites tumors in mice, two strains of which grow in rats and golden hamsters in the ascites form. It is shown that various experimental manipulations lead to changes in the biology of the tumors. Transformation into the ascitic form, heterologous growth and treatment with various agents act as mechanisms in the selection of tumor cells with specific characteristics. This is evidenced by the different chromosome numbers, different biochemical properties and by the appearance of specific resistance. Abrupt changes in the biology of transplanted tumors may be produced by known or unknown mechanisms of selection.

63-1406 CHANGES IN THE GROWTH AND VIRULENCE OF TRANSPLANTED TUMORS IN RATS OBSERVED OVER A LONG PERIOD. (Ger.)

Matthies, E. (Pharmacol. Inst., Martin-Luther-U., Halle-Wittenberg, Germany) and J. E. Peters. Acta Biol. Med. Germ. 10(3-4):375-386, 1963.

The rate of tumor formation, latent period, host survival time and tumor size of a group of transplantable tumors were studied and evaluated statistically in 3415 male and female albino rats

during the yr. 1955-1961 in the case of the Jense and Yoshida sarcoma, the Guerin carcinoma as well as the Walker tumor of the rat. It was found that the incidence of tumor formation is not a fixed biological constant but rather is subjected to changes over the yr. Only the two most virulent ("young") tumors maintained their rate of incidence while the less virulent ("old") tumors showed a decrease during the report period. However, the incidence of the tumor formation was found adequate for purposes of comparison. Virulence of the graft tumors studied, ranked in the order of decreasing virulence, was in the following sequence: Guerin, Yoshida, Jensen and Walker. Considerations of metastases formation, survival time and tumor size may also contribute indirectly to an assessment of tumor virulence. Seasonal variations of virulence were observed with the Walker tumor and the Yoshida sarcoma. With the former, the max. incidence of tumor formation occurred in the summer, while the latter reached its max. in the winter.

63-1407 CHROMOSOMAL ALTERATION OF ERYTHROPOIETIC CELLS IN CHRONIC MYELOID LEUKEMIA. (E.)

Trujillo, J. M. (Dept. Biol., City Hope Med. Ctr., Duarte, Cal.) and S. Ohno. Acta Haemat. 29(5):311-316, 1963.

Karyotype analyses of fresh bone marrow of a pt. in the acute terminal phase of chronic myeloid leukemia revealed the presence of a Ph¹ chromosome in 67 of 71 metaphase figures with 46 chromosomes. It was also found in all 25 metaphase figures of cells with 47 chromosomes, considered a secondary stem line with an extra element in the group of smaller acrocentrics. The data suggests a common ancestor for both erythropoietic and granulopoietic elements.

63-1408 INFLUENCE OF SECONDARY INFECTION ON TUMOR HOST SERUM-BOUND CARBOHYDRATES.

(E.) Patterson, M. K., Jr. (Samuel Roberts Noble Found., Ardmore, Okla.), M. D. Maxwell and T. A. McCoy. Proc. Soc. Exp. Biol. Med. 113(3):689-691, 1963.

In male Holtzman rats bearing Walker 256 carcinoma sarcomas which were infected with Salmonella typhimurium, the serum-bound hexose was increased or unchanged (140 and 153 mg%) compared to levels in hosts bearing "bacteria-free" tumors (111-125 mg%; untreated control 128 mg%). The change in bound carbohydrates of the "contaminated" hosts was evident in 3 days, prior to any visible tumor growth. A similar effect was obtained by use of lipopolysaccharide extracted from S. typhimurium. No effects were seen when extracts from normal tissue or "bacteria-free" tumors were inj. into hosts. There was an extended lag in growth of "contaminated" tumors; survival time in the "bacteria free" group was shorter.

-1409 THE CHANGES OF BIOLOGICAL PROPERTIES AND MORPHOLOGICAL STRUCTURES OF THE TRANSPLANTABLE RABBIT SARCOMA STRAIN DURING 100 GENERATIONS. (Rus.) Kondrat'eva, A. F. (Inst. Col., Acad. Med. Sci. USSR, Moscow). Vop. kol. 9(7):11-15, 1963.

strain of osteogenic sarcoma obtained during transplantation of an induced sarcoma, after 1 yr. has passed through 100 generations of rabbits, with 754/936 (80.6%) positive takes. Incidence of takes was 38.5% in passage (P) 1-5; 55.7-78.7% in P 6-25; 91.5-96.9% in P 26-35 (maximum); and 85.2-90.1% in P 36-100. Time of appearance of the tumor was 17.1-19.9 days for P 1-10; 10.5-15.4 days for P 11-25; 7.4-9.4 days for P 26-40; and 9-10 days for P 40-100. Tumor growth was rapid, with survival in P 40-100 of 1-45 days. Metastases to the lung was 100% in P 1-15; 42.1-44.3% in P 16-26; 29.4-30.5% from P 27-40; and 10-15% from P 56-100. Over the period of observation, the tumor changed gradually in the direction of a simpler, more undifferentiated structure. The tumor was found to be a polymorphocellular sarcoma with well marked cellular and nuclear polymorphism. With progressive transplantation it was found to lose its ability to form osseous structures. The tumor has a massive blood supply.

-1410 THE CELL DIVISION PATTERN OF MAMMARY GLAND EPITHELIUM AT VARIOUS STAGES OF THE ESTRUS CYCLE IN MICE OF HIGH AND LOW CANCER INCIDENCE. (E.) Laguchev, S. S. (Inst. Exp. Biol. USSR, Moscow). Biull. Eksp. Biol. Med. (Eng.) 3(3):318-321, 1963.

In a study of mitotic activity of the mammary gland and epithelium, virgin mice were examined in various stages of the estrus cycle. For the low cancer strain, mean mitotic coefficients (divisions/1000 cells) during estrus and diestrus were 3.18 (range 1.3-6.66) and 0.66 (range 0-5.66). For the C3H high cancer strain, mean mitotic coefficient during estrus was 3.41 (range 0.66-12.33), during diestrus 3.94 (range 0-17.33). Because of the wide range in values, it is difficult to decide whether hormonal regulation of mitotic activity was disturbed in all C3H mice. It may be assumed that in many C3H females, mitotic activity either changes very little in different stages of the estrus cycle, or in some cases is higher in diestrus than in estrus.

-1411 TUMOUR FORMATION OF PITUITARY ISOGRAFTS IN MICE. (E.) Röpcke, G. (Netherlands Cancer Inst., Amsterdam), L. M. Pot, H. G. Kwa and O. Mühlbock. Acta Un. Int. Cancr. 19(3-4):704-705, 1963.

pituitary isografts in intact female mice to sites remote from the hypothalamus grow progres-

sively and become tumorous, reaching a size of up to 500x the amount of tissue implanted. Factors governing the growth rate were found to be: (a) the genetic constitution of donors and hosts; (b) the site of implantation; (c) age of the donors. All tumors, regardless of the experimental conditions, produced prolactin continuously. Between the experimental groups the amount of prolactin produced was proportional to the size of the grafts. Within the experimental groups marked variations in size were observed. Morphologically the pituitary isografts were similar to the pituitary adenomata induced by estrogen treatment and to the spontaneous prolactin-producing pituitary tumors observed occasionally.

63-1412 DUODENAL CANCER IN HAMSTERS INDUCED BY A TRANSPLANTABLE HUMAN CANCER OF THE COLON. (E.) Patterson, W. B. (Pondville Hosp., Walpole, Mass.). Acta Un. Int. Cancr. 19(3-4):640-643, 1963.

In a strain of hamsters (Pondville) with a low incidence of spontaneous tumors, 2/370 bearing transplants of a human cancer of the colon (B-10) developed carcinomas of the small bowel, 2 others developed papillary adenomas with invasion. Time of appearance of the tumors was between 21-56 days. These cancers were not seen in animals bearing other transplanted human tumors. It is suggested that this particular colon cancer induces cancer in the host animals by the elaboration of a circulating growth factor.

63-1413 INDUCTION OF RETICULAR TUMORS IN MICE BY REPEATED ANTIGENIC STIMULATION. (E.) Metcalf, D. (Walter and Eliza Hall Inst., Melbourne, Australia). Acta Un. Int. Cancr. 19(3-4):657-659, 1963.

Prolonged antigenic stimulation in C3H mice using Salmonella flagellar antigen or bovine serum albumin resulted in a moderate increase in the incidence of lymphoid leukemia, reticulum cell sarcomata and plasma cell tumors. These neoplasms were transplantable to C3H recipient mice, but their progressive growth in the recipient mice was not dependent on continued antigenic stimulation.

63-1414 STUDIES ON PREDISPOSING FACTOR IN EXPERIMENTAL OVARIAN TUMORIGENESIS. (E.) Mody, J. K. (Indian Cancer Res. Ctr., Parel, Bombay, India). Acta Un. Int. Cancr. 19(3-4):759-761, 1963.

In a review of the author's work, structure changes in the ovaries of IF mice are described after (a) repeated spontaneous pseudopregnancies, (b) olfactory lobectomy, and (c) after multiple sterile matings. It is concluded that the data are useful in explaining the greater susceptibility of IF strain mice to experimental ovarian tumorigenesis.

- 63-1415 ENDOGENOUS CARCINOGENS FOR THE EXTRA-HEPATIC BILIARY TRACT. (E.) Fortner, J. G. (Mem. Sloan-Kettering Cancer Ctr., New York) and H. T. Randall. Acta Un. Int. Cancr. 19(3-4):629-631, 1963.

Two cats implanted with gallstones from a pt. with primary cancer of the gallbladder developed primary adenocarcinomas of the gallbladder; stones had been in situ for about 5 yr. and 8 mo. Gallstones from a pt. with breast cancer upon implantation into the gallbladder of a cat resulted in papillary hyperplasia with atypical foci. An adequate comparison of the effects of gallstones from pts. of test and control groups was impossible because too few cats survived a sufficient period of time. However, it is evident that chronic inflammatory changes are not in themselves carcinogenic.

- 63-1416 RH-FACTORS OF BLOOD AND THEIR RELATIONSHIP WITH CANCER. (E.) Mitra, S. (Chittaranjan Natl. Cancer Res. Ctr., Calcutta, India) and A. Basu. Naturwissenschaften 50(14):504, 1963.

In a study of the relation of the Rh factor to cancer of the digestive system, among female pts., 16/16 were Rh + ve, in males 4/26 were Rh - ve, to give an Rh - ve incidence for both sexes of 9.5%. In the total cancer group of 936 pts., Rh - ve incidence was 4.07% compared to 3.57% in 378 normal subjects and non-cancer pts. In contrast to other reports, cancer of the digestive system is more prevalent among Rh negative males in Calcutta (15.38%) than cancer in other

sites studied (genital, 4%; buccal cavity + pharynx, 4.25%; respiratory system, 2.55%; and others, 4.65%).

- 63-1417 THE RELATIONSHIP BETWEEN BLOOD GROUP A AND GASTRIC CANCER. (E.) Tan, A. I. (Dept. Med., U. St. Thomas Hosp., Philippines). J. Philipp. Fed. Priv. Med. Prac. 11(5):428-431, 1963

Among 100 pts. with gastric carcinoma, incidence of those with type 'O' blood was 30%; with type 'A' blood 39%; with type 'B' blood 25%; and with type 'AB' blood 6%. In a series of 100 pts. with extra-gastric carcinoma, incidences were, resp.: 51%, 20%, 26% and 3%. In 500 consecutive cases with various diseases, incidences were, resp.: 46.2%, 24.8%, 28.8% and 3.2%. Thus the frequency of type 'A' blood among gastric carcinoma pts. was greater than among 'O' pts. The frequency of 'A' blood was 19% over that of extra-gastric carcinoma pts. and 14.2% over cases with other diseases.

- 63-1418 BLOOD GROUPS AND LEUKEMIA IN CHILDREN. (It.) Cordone, G. (Inst. Clin. Pediat., U. Genoa, Italy) and F. Tavella. Minerva Pediat. 15(19-20):631-633, 1963.

Among 102 children with leukemia, incidence in those with group 'O' blood was, 58.8%; group 'A' 25.5%; group 'B', 12.7% and group 'AB', 2.9%. Composition of the blood groups in healthy controls was, resp.: 46%, 42.3%, 9.4% and 2.3%. The incidence of leukemia in subjects belonging to blood group 'O' was significantly increased.

ERRATA

- 1(2):#168, 1963, Correct second author's name to read N. N. Litvinov.
1(3):#413, 1963. Line 11, change 3 mg to 30 mg.
1(4):#675, 1963. Line 4, change \pm to $+$.

- 1(5), 1963. Author Index, under Bernard, J., delete 871. Add Bernhard, J. 871.
1(5), 1963. Author Index, change Kelley, M. G. to Kelly, M. G.

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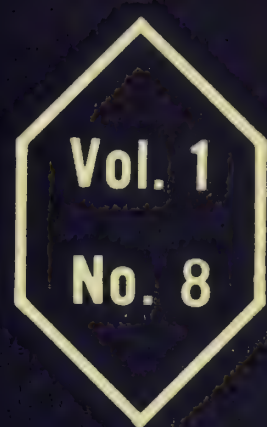
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Chap. 10

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CARCINOGENESIS
ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service

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Volume 1, Number 8
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1419-1632

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration(s)	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health, USA
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit(s)
e.g.	for example	ppm	parts per million
FFU	focus forming unit(s)	pt.(s)	patient(s)
g	gram(s)	RBC	red blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin.	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
ID ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution(s)
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit(s)
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose(s)	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

1419 TRANSFORMATION OF HUMAN AND ANIMAL TISSUES AFTER VIRUS INFECTION (SUMMARY). NEOPLASTIC TRANSFORMATION INDUCED IN RO BY POLYOMA VIRUS. (E.) Stoker, M. (Inst. Virol, U. Glasgow, Scotland). Proc. Roy. Soc. Med. 56(4):251-252, 1963.

Brief review, chiefly of work from the author's laboratory. (See CRA 1(1):#116; ibid., (3):#468; ibid., (5):#790, 1963.) (7 references)

1420 THE ENVIRONMENT IN RELATION TO CANCER. (E.) Wade, L. (Sloan-Kettering Inst. Cancer Res., New York). Arch. Environ. Health (Chicago) 7(2):172-178, 1963.

Review and discussion of the nature of cancer and its relation to environmental factors. The multiplicity of suspected environmental factors and their ubiquity, plus the possibility that the same factors may have desirable biological effects under some circumstances, renders efforts to eliminate them from the environment both futile and suspect. It is suggested that those concerned with environmental carcinogenesis should direct attention to the individual who does not develop clinical cancer under circumstances where the occurrence of the disease is common. What peculiarities of the host and his environment are responsible for his failure to manifest the disease? (21 references)

1421 NEW CONSIDERATIONS ON THE USE OF IONIZING RADIATIONS IN MEDICINE. (Fr.) Roth, J. (Natl. Ctr. Sci. Res. (CNRS), Paris). Path. Gen. 63(747):485-492, 1963.

Review and discussion of the dangers in the use of ionizing radiations, and the added hazards due to fallout residues from thermonuclear explosions and from other atmospheric pollution. (22 references)

1422 CANCER AND VIRUS. (Fr.) Lépine, P. (Virus Serv., Pasteur Inst., Paris). Lyon Med. 12(5):235-246, 1963.

Review devoted largely to tumors of birds, rats and mice, it is stated that in certain animal tumors, in fact all those which have been studied thoroughly, there are close associations with viruses. There are some malignant tumors having all the characters of cancer in which it is possible to detect constantly an agent having the attributes of a virus. The study of certain of these tumors has dramatically altered the concept of cancer by showing the existence of dormant viruses which, under the influence of associated factors, genetic or hormonal, sometimes with the intervention of external

carcinogenic factors, give rise to cancers. The questions are raised as to whether cancer can be included in the field of infectious diseases and also how widely can the viral origin of cancer be applied. (No references)

63-1423 PREVALENCE OF CANCER OF THE LUNG.

(Pol.) Kozłowa, E. W. (P. A. Herzen Res. Inst. Oncol., Moscow) and W. W. Rodionow. Nowotwory 13(3):233-243, 1963.

Polish translation of a Russian review of foreign and Soviet literature on the incidence of pulmonary cancer during the last 100 yr. Charts on the autopsy diagnoses by various authors, the incidence and mortality rate in larger Ukrainian cities, the Russian Federated Republic and U. S. A. are presented. Between 1948-1954, in the Ukraine there were 7.3-16.1 cases of pulmonary cancer per 100,000 of the male population, and 1.5-3.0 of the female population. In the Russian Republic in 1960, incidence of cases (per 100,000) for males and females was 21.6 and 4.8, resp.; mortality rates were 31.2 and 8.2, resp. It is concluded that the incidence of the cancer of the lungs increased 7x between 1910 and 1954. (54 references)

63-1424 THE ROLE OF CHROMOSOME ANOMALIES IN CANCER. (E.) Koller, P. C. Ciba Sympos. 11(2):54-63, 1963.

A brief review and discussion is presented of changing concepts relative to the role of chromosome anomalies in cancer. Much evidence has been accumulated to support the view that, in ascites tumors, the development of cell variants showing different chromosome numbers can be attributed to environmental conditions. There is no consistent pattern in regard to the relationship of changes in chromosomal pattern and malignancy. Changes which occur in induced primary tumors can also be related to changes in environmental conditions or to toxicity of the agent. Recent studies have emphasized the fact that cancer cells may display extreme variability in respect to their chromosomes without impairing their vitality or proliferative capacity. Hence, in contrast to "normal" cells, the conclusion to be drawn is that malignant cells do not require a normal and genetically fully balanced chromosome environment for survival. The higher incidence of leukemia in mongols may be due to the "metabolic instability" created by the extra chromosome seen in some of these cases. (No references)

63-1425 PLASTICS IN PLASTIC SURGERY: A REVIEW OF THE CARCINOGENIC PROBLEM. (E.) Arons, M. S. (Dept. Plastic Surg., U. Texas Med. Branch, Galveston). Texas Rep. Biol. Med. 21(2):163-167, 1963.

A brief review is presented of the carcinogenic potential of implanted plastic materials. It is stated that no conclusion can be drawn from the information available at the present time. (29 references)

63-1426 AIR POLLUTION AND LUNG CANCER. (E.) Kotin, P. (NCI, Bethesda) and H. L. Falk. Pp. 140-142 in Natl. Conf. Air Pollution. Proceedings. Dec. 10-12, 1962. Washington, D. C. U. S. Public Health Serv. Publ. No. 1022. Washington, D. C., U. S. GPO., 436 pp., 1963. \$2.75.

A synthesis of various studies suggests that the carcinogenic properties of polluted urban atmosphere provide at least 2 indispensable links in the pathogenesis of lung cancer. (1) The environmental presence and the host entry of agents proved experimentally to be carcinogenic and epidemiologically associated with increased liability to the development of lung cancer. (2) The occurrence in the atmosphere of host-modifying factors which facilitate deposition and abnormal retention of particulate matter in the lungs by an effect on the ciliated mucus-secreting epithelium. Periodic denudation of the superficial epithelium by atmospheric irritants can provide a favorable environment for abnormal growth in the presence of a carcinogenic stimulus. Much experimental evidence is especially meaningful by virtue of its quantitative compatibility with the pattern of diseases seen in human populations at risk. There exist, however, numerous apparent inconsistencies when quantitative extrapolation of the experimental data is attempted. Various studies are detailed which attempt to explain or elucidate the basis for these inconsistencies, studies related to anticarcinogenesis, the effect of multiple exposure, and factors which alter the metabolism of carcinogenic hydrocarbons. Other factors briefly considered are the role of promoting agents, presence of other diseases, and occupational factors. (See also CRA 1(4):#614 and ibid., #640, 1963.) (No references)

63-1427 PREPARED DISCUSSION: AIR POLLUTION AND LUNG CANCER. (E.) Wynder, E. L. (Sloan-Kettering Div., Cornell U. Med. Coll., New York) and D. Hoffmann. Pp. 143-148 in Natl. Conf. Air Pollution. Proceedings. Dec. 10-12, 1962, Washington, D. C. U. S. Public Health Serv. Publ. No. 1022. Washington, D. C., U. S. GPO., 436 pp., 1963. \$2.75

Recent and current investigations designed to elucidate some of the apparent excess of lung cancer which may be related to an "urban factor" are reviewed and discussed. While a correlation of an "urban factor" to lung cancer appears to be established, the extent to which this factor may be due to air pollutants remains to be proven. The composition of the exhaust of

various internal combustion engines, the influence of the type of fuel and various climatic conditions, the role of promoting substances or the carcinogenic activity of some polynuclear aromatic hydrocarbons in such exhaust are with areas undergoing investigation. Cilia-static agents known to be present in both general air pollutants and in cigarette smoke can affect the flow of mucus and thus affect the resorption of various components in air pollutants as well as in tobacco smoke. (9 references)

63-1428 MALIGNANT TRANSFORMATION BY POLYOMA VIRUS. (E.) Habel, K. (Natl. Inst. Allergy Infect. Dis., Bethesda). Ann. Rev. Microbiol. 17:167-178, 1963.

A review and evaluation is presented of the most important recent research concerning mechanism of polyoma virus transformation, the relationships between virus and the cell after transformation, and some of the virus-specific properties of the transformed cells. These items are discussed for both in vivo transformation and for that occurring in in vitro systems. (50 references)

63-1429 ON THE NATURE OF THE HERITABLE CHANGES LEADING TO AUTONOMOUS GROWTH IN CERTAIN NEOPLASTIC CELL TYPES. (E.) Braun, A. C. Pp. 108-117 in Perspectives in Virology III. The Gustav Stern Symposium. Pollard, M. (Ed.) Hoeber Med. Div., Harper & Row, Publ., Inc., New York, 292 pp., 1963.

In a discussion and review chiefly of certain neoplastic plant cells, the author presents evidence that heritable changes in the cell may be associated with extranuclear, rather than nuclear material. It has been shown that all cells in the teratoma induced by a factor in the crown gall bacterium are tumorous. However, by forcing tumor shoots into rapid organized growth by a series of graftings to healthy plants, such tumor shoots gradually recovered and ultimately became normal in every respect. These studies clearly demonstrate that the crown gall tumor cell contains, potentially at least, all of the genetic and non-genetic factors present in the normal cell. It is clear that some fundamental cellular mechanism is involved in the simultaneous or perhaps sequential activation of the diverse biosynthetic systems found to be permanently unblocked in the plant tumor cell. Studies designed to characterize that mechanism in the plant cell indicate 6 of 7 biosynthetic systems studied are ion-activated. (3 references)

63-1430 INFECTION AND LEUKAEMIA. (E.) Lancet 2:288, 1963.

The possible infectious origin of leukemia is discussed, based chiefly on the study of incidence

the town of Niles, Illinois by Heath and Terlik (see CRA 1(5):#978, 1963). Other studies related to restricted areas or families are cited. In a survey of leukemia in West Wall between 1948 and 1959, 2 towns had incidences of 28.8 and 13.9 per 100,000. In another survey by counties, the only high incidence of leukemia was in sparsely populated Montgomeryshire. (5 references)

1431 PRODUCTION AND PROPERTIES OF TRANSPLANTABLE TUMORS OF THE THYROID GLAND IN THE FISCHER RAT. (E.) Wollman, S. H. (Natl. Cancer Inst., Bethesda). Pp. 579-618 in Recent Progress in Hormone Research. Proceedings of the 1962 International Hormone Conference. Pincus, G. (Ed.). Academic Press, New York and London, 1963.

An extensive review is presented of work from the author's laboratory on the various aspects of the production of transplantable thyroid gland tumors in the Fischer rat. In relation to characteristics of successive generations, some of the studies reported were on growth rate, generation time, ^{131}I metabolism and effects of hypophysectomy or thiouracil feeding. Other studies included work on the nature of iodoproteins in tumor bearing line 1-8, properties of tumors of line 1-5A, sialic acid in thyroid tumors and gland, autoradiographic studies and various studies of the movement of ^{131}I in tumor and host. It is obvious from the experimental material that not only are thyroid tumors of different lines distinguishable from each other, but individual tumors them-

selves are frequently heterogeneous. The observations can be taken as illustrative of the well known finding that many kinds of tumors can be derived from a single tissue. This generalization is a useful supplement to Greenstein's generalization that tumors derived from different tissues are more similar than the tissues of origin. (46 references)

63-1432 LEUKEMIA IS A DISEASE OF VIRAL ETIOLOGY. (Sp.) Mas y Magro, F., Jr. (de Calvo Sotelo St., 12. Alicante, Spain). Arch. Med. Exp. (Madrid) 24(3-4):155-169, 1961.

A review is presented of the evidence for the viral etiology of leukemia. (No references)

63-1433 THE SEARCH FOR HUMAN TUMOR VIRUSES. (E.) Dmochowski, L. (U. Texas M. D. Anderson Hosp., Houston). Texas Rep. Biol. Med. 21(2):114-135, 1963.

A review (with some unpublished observations included) is presented of early and recent work which has culminated in the association of viruses with many animal tumors. The mammalian cell-virus relationships, especially as regards the nucleic acids, are explored in an introductory section. Many animal tumor viruses are discussed in the light of a model system which could be used in the search for human tumor viruses. A final section explores infectious animal and human viruses and their relation to human tumors. (147 references)

See also abstract no.: 1576

- 63-1434 LYMPHOCYTIC LEUKEMIA -- MAN AND ANIMAL. (E.) Ofuji, T. (Dept. Int. Med., Okayama U. Sch. Med., Japan) and H. Sunami. Acta Haemat. Jap. 25(3-4):294-317, 1962.

It is possible to differentiate the lymphoblast from the other blast cells by the simultaneous use of various technics including May-Giemsa staining, vital observation, fluorescence microscopy and the Brachet test, of which the latter two appear to be of greatest value. Lymphocytic leukemia induced in mice by X-irradiation or 20-methylcholanthrene appears to have a multicentric origin, first in the spleen or thymus, and then in the lymph nodes. It has been shown that hypoplasia of the hematopoietic organs precedes the development of a full-blown leukemia. During cell-free passage of viral leukemia in mice, a transformation of the leukemic form from lymphocytic to myelogenous has been seen occasionally. As an explanation for such a phenomenon, it is suggested that 2 distinct viruses responsible for each type of leukemia could coexist in a host. A transition of lymphosarcoma into lymphocytic leukemia in man and animals has been confirmed by tissue culture of the hematopoietic organs.

- 63-1435 OBSERVATIONS ON SUBCUTANEOUSLY IMPLANTED POLYETHERURETHANE SPONGE IN MICE. (E.) Dunaif, C. B. (Dept. Surg., New York Hosp.-Cornell Med. Ctr., N.Y.), W. T. Stubenbord and H. Conway. Surg. Gynec. Obstet. 117(4): 454-458, 1963.

Polyetherurethane sponge was implanted beneath the mammary glands of 132 noninbred Swiss albino mice for the purpose of studying its carcinogenic potential. After 1 yr., examination of 104 surviving mice failed to reveal tumor in association with the implants. Shortly after insertion, the sponge implants elicited a foreign body reaction, which eventually resulted in their shrinkage and distortion. (Author summary)

- 63-1436 MALFORMATION OF THE EXTREMITY IN THE MOUSE FOETUS CAUSED BY X-RADIATION OF THE MOTHER DURING PREGNANCY. (E.) Murakami, U. (Res. Inst. Environ. Med., Nagoya U., Japan), Y. Kameyama and H. Nogami. J. Embryol. Exp. Morph. 2(Part 3):549-569, 1963.

Different groups of the ddN strain mice were exposed to X-radiation of 300 r, 200 r and 150 r from the 8th to 13th day of pregnancy. The highest incidences of malformations of the extremities were found in the offspring of mothers treated on days 11 or 12 of pregnancy with 200 r or more. The formation of ectrodactylia after X-radiation began with cellular necrosis in the hand and foot plate corresponding to the predominant site of ectrodactylia, i.e., chiefly in

the second digit of the fore-limb and in the third digit of the hindlimb. The process may damage the precursor of the pre-cartilage. In contrast to the regenerative neural tissue, compensation does not take place in the mesenchymal tissue once the destruction is severe, and the reduction of digits will therefore persist. The effect of X-radiation upon a developing digital primordium may be a directly destructive process. The critical stage for extremity malformations due to thalidomide in human beings corresponds with the critical stage for X-ray malformations of the extremities in mouse.

- 63-1437 LEUKEMIA INCIDENCE AND LONGEVITY IN RADIATION-INDUCED HOMOLOGOUS MOUSE CHIMERAS. (E.) Davis, W. E., Jr. (U.S. Naval Radiol. Defense Lab., San Francisco, Cal.), L. J. Cole, W. A. Foley and V. J. Rosen, Jr. Radiat. Res. 20(1):43-52, 1963.

In connection with studies on lymphoid cell chimerism and homograft tolerance in long-lived homologous (allogeneic) radiation chimeras, data have been collected on life span and on occurrence of leukemia and other lesions. The chimeras were (C57L x A)F₁ hybrid mice (10 to 12 wk. old) exposed to 880 rads of X-radiation and inj. with bone marrow cells from C3H donors. Out of a total of 119 mice combined from several subgroups 65% were dead by age 32 wk. (20 wk. after marrow inj.), with gross symptoms of secondary disease evident in the great majority. Relatively few deaths occurred between 32 and 75 wk., and the max. life span was 105 wk. Leukemias were observed in 5 out of 54 (9%) homologous chimeras, but none were found in the isologous chimera group.

- 63-1438 CARCINOMATOUS COMPLICATION IN RADIO- DERMATITIS. (E.) Malbec, E. F. (Ramos Mejia Hosp., Buenos Aires, Argentina), J. V. Quaife and H. A. Vieyra Urquiza. Plast. Reconstr. Surg. 32(4):447-450, 1963.

A brief comment on the histology and pathogenesis of malignant degeneration in radiation burns is followed by a description of the authors' series of 12 neoplastic complications out of 82 cases. Time elapsed between irradiation and biopsy of the suspected lesion in 6 cases was between 5-10 yr.; in 4 cases, 12-15 yr.; in the remaining 2 cases, 17 and 21 yr. One tumor was a spindle cell carcinoma, the others were epidermoid carcinomas. In all cases radiotherapy was applied for cosmetic reasons. Biopsy seems to be the only means to correct diagnosis before it is too late for radical excision. It is suggested that the incidence of chronic radiodermatitis and therefore cancer, its most dangerous complication (14.39%), might be reduced if doctors limited the indication of radiation therapy to those diseases in which no other treatment is available.

1439 CLINICAL INVESTIGATIONS ON THE URINARY 17-KETOGENIC STEROIDS. IV. STUDIES ON CHANGES OF URINARY 17-KETOGENIC STEROIDS EXCRETION BY AGE DURING ADOLESCENCE OF THE CHILDREN EXPOSED TO THE ATOMIC BOMB IN UTERO. (E.) Arai, Y. (Dept. Int. Med., U. Kyoto, Japan). Naika Hokan (Jap. Arch. Intern. Med.) 10(5):235-243, 1963.

The determination of urinary 17-ketogenic steroids (17-KGS) was performed in 275 adolescents born from a group of 874 children who were either exposed to the atomic bomb in utero in Nagasaki or who entered the city after the bombing (non-exposed). The measurements were made on the same subjects between the age of 13 and 18 and at intervals of 3 mo. While there were no differences in 17-KGS excretion in relation to age and sex, there were no significant differences between exposed and non-exposed subjects. Among the exposed subjects there were no significant differences between those exposed at less than 2,000 meters from the hypocenter, compared to those exposed at 2,000-5,000 meters; there also were no significant differences in relation to the trimester of pregnancy in which exposure occurred. Results indicate an absence of effect of atomic bomb radiation on the adrenocortical function of adolescents who were exposed in utero.

1440 THE SEQUELAE OF IRRADIATION FOR BENIGN CONDITIONS. (E., Abstract) Cannon, B. (Mass. Gen. Hosp., Boston) and J. E. Murray. Derpta Med. Sect. 9(58):113-114, 1963.

A total of 165 cases from the records of the Massachusetts General Hospital, the Peter Bent Brigham Hospital and from personal files has been reviewed. In each, surgical treatment was performed or recommended for the sequelae of therapeutic irradiation in benign conditions or accidental exposure. Several interesting observations have been made. Twice as many cases were seen in the decade 1948-1957 as in the preceding decade. Nineteen per cent of the total had a proven diagnosis of carcinoma, about equally divided between basal cell and squamous cell types, contrary to the usual teaching. With only one exception, all basal cell carcinomas occurred in the face, and 75% of these occurred following treatment for acne. The av. latent period for all carcinomas treated was 28 yr.

1441 MATHEMATICAL-BIOLOGICAL APPROACH TO THE PROBLEM OF RADIATION-INDUCED CARCINOGENESIS. (E.) Bernard, S. R. (Oak Ridge Natl. Lab., Tenn.). Health Phys. 8(4):459, 1963.

Theoretical predictions of the percentage of spontaneous leukemia incidence which can be attributed to natural background radiation and the effective rem dose-rate to produce 100% incidence made with the linear theory (single-theory) of Lewis and the quadratic theory of others are in marked disagreement. From the

quadratic theory it is estimated that approx. 0.04% of the natural cases of leukemia can be attributed to background radiation and an effective rem dose-rate of approx. 100 rems/yr. for a period of 70 yr. is required to produce 100% incidence. From the linear theory it is estimated that approx. 10% of the natural cases are due to background radiation and an effective dose rate of approx. 1 rem/yr. for a period of 70 yr. is required to produce 100% incidence.

63-1442 TOXICITY OF PLUTONIUM IN MICE. (E.) Finkel, M. P. (Argonne Natl. Lab., Ill.) and B. O. Biskis. Health Phys. 8(6):565-579, 1962.

Groups of CF No. 1 female mice given graded doses of plutonium citrate (0.04-40.6 $\mu\text{C/kg}$, i.v.) reduced life expectancy, decreased hemoglobin and leukocyte conc. in the peripheral blood, increased the incidence of liver degeneration, and induced osteogenic sarcomas. In none of these respects were the lowest dosage groups, 0.04 and 0.08 $\mu\text{C/kg}$, different from the control group. (Author summary)

63-1443 THE SKELETAL TOXICITY OF Pu^{239} IN ADULT BEAGLES. (E.) Jee, W. S. S. (Dept. Anat. Radiol., U. Utah Coll. Med., Salt Lake City), B. J. Stover, G. N. Taylor and W. R. Christensen. Health Phys. 8(6):599-607, 1962.

Plutonium²³⁹, in i.v. doses of 2.8, 0.90, 0.30 and 0.096 $\mu\text{C/kg}$ induced 7/9, 12/12, 12/12 and 7/8 bone cancers, resp., in adult beagles. The av. accumulated rads to the skeleton varied from 326 ± 70 to 6470 ± 1590 . The osteogenic sarcomas appeared later at lower dose levels and absorbed skeletal radiation doses. Multiple primary osteogenic sarcomas varied from 0 to 7 tumors/dog. Sixty-eight per cent of the tumors originated from the spongiosa of extremities (36.7%) and the vertebral column (32.7%). A total of 93.9% (92/98) tumors arose from spongy bone, while only 6.1% (6/98) originated from cortical bone. The anatomical distribution of osteogenic sarcomas differed for each dose level. A fibrosarcoma and a squamous cell carcinoma involving the skeleton were detected in the 0.096 $\mu\text{C/kg}$ group. Radiochemical analyses of individual bones showed extreme variation in plutonium conc. from bone to bone and within individual bones. The skeleton exhibited extensive gross tissue damage in the higher dose levels, while only isolated empty lacunae in trabeculae and canal plugs and loss of osteocytes in cortical bone were observed in the 0.096 $\mu\text{C/kg}$ group. (Author summary)

63-1444 LIVER INJURY IN BEAGLES WITH Pu^{239} : DISTRIBUTION, DOSAGE AND DAMAGE. (E.) Cochran, T. H. (Dept. Anat. Radiol., U. Utah Coll. Med., Salt Lake City), W. S. S. Jee, B. J. Stover and G. N. Taylor. Health Phys. 8(6):699-703, 1962.

The livers of Pu²³⁹-injected beagles retained 15-30% of the inj. dose (0.1, 0.3, 0.9 and 3.0 $\mu\text{C/kg}$). Initially, autoradiographs showed a uniform distribution of α -activity. At 400 days post-injection, there was a focal distribution associated with condensed reticulum and reticulo-endothelial conc. Subsequently, at the time of sacrifice 3-8 yr. post-injection, 60-85% of the liver was replaced by regenerative nodules with no α -activity. The absence of hepatomas was in sharp contrast to the presence of osteogenic sarcomas in some dogs with comparable doses to bone and liver. (Author summary)

- 63-1445 FURTHER STUDIES ON LUNG CANCER FROM $\text{Ce}^{144}\text{F}_3$. (E.) Cember, H. (Kettering Lab., U. Cincinnati Coll. Med., Ohio). *Health Phys.* 9(5):539-544, 1963.

Cerium 144 as 1 μ -diameter $\text{Ce}^{144}\text{F}_3$ particulates produced lung cancer in rats when intratracheally inj. at dose levels of 0.5, 1, 2 and 4 μC . The tumor frequency in each of these treatment levels was 8/41, 6/44, 4/34 and 14/42, resp. In the lowest dose level, the first death due to lung cancer, a lymphosarcoma, occurred 528 days after exposure. The radiation dose to the lungs in this case was 600 rads. Insofar as extrapolation of these experimental data to man is valid, the results of this experiment imply that the radio-toxicity of atmospheric Ce^{144} is greater than that assumed at the present time. (Author summary)

- 63-1446 EFFECTS OF HEAVY HIGH ENERGY CHARGED PARTICLES. II. PRIMARY ATYPICAL EPITHELIAL HYPERPLASIA IN MOUSE SKIN AFTER EXPOSURE TO 10 MEV PROTONS, 20 MEV DEUTERONS, OR 40 MEV α -PARTICLES. (E.) Lippincott, S. W. (Bowman Gray Sch. Med., Winston-Salem, N.C.), J. E. Jesseph, C. P. Baker, W. G. Calvo, C. R. Jansen, K. R. Rai and V. Alcober. *Arch. Path. (Chicago)* 76(5):527-536, 1963.

A more detailed account of the paper abstracted as CRA 1(5):#811, 1963.

- 63-1447 LATE EFFECTS IN MAMMALS. CARCINOGENESIS. (E.) Loutit, J. F. (Med. Res. Coun. Radiobiol. Res. Unit, Harwell, Didcot, Berkshire, England). Pp. 372-390 in *Radiation Effects in Physics, Chemistry and Biology*. Proc. 2nd Internatl. Congress Radiat. Res., Harrogate, Gr. Britain, August 5-11, 1962. Ebert, M. and A. Howard (Eds.). North-Holland Publ. Co., Amsterdam, 510 pp., 1963.

The highlights of 17 papers presented to the congress are reviewed. Concerning external irradiation, L. J. Cole and P. C. Nowell, showed in small numbers of LAFl mice a higher incidence of leukemia after fractionated doses of X-rays, 5 rad x 52 wk. compared to 260 rad at one time (see CRA 1(4):#620,

1963). N. Trainin and I. Berenblum consider radiation as initiator and urethan as promoter in a 2-stage process of leukemogenesis. They found that a tissue from a thymectomized, irradiated mouse was found to contain a "transmissible factor" which when inj. into intact recipients which were then treated with urethan, caused 10% of the mice to develop "leukemia" within 9 mo. C. J. Shellabarger, G. E. Aponte, E. P. Cronkite and V. P. Bond showed that in Long Evans rats, sublethal total body irradiation of intact, young females markedly increased incidence of mammary tumors. M. R. Sikov and J. E. Lofstrom reported that Sprague-Dawley rats X-irradiated with 20 or 100 r on intra-uterine day 10 and with 50 or 185 r on day 15 showed an increase in the number of mammary tumors in offspring, but this occurred late in life, while Shellabarger reported early development of tumors in rats irradiated as adolescents. H. H. Vogel, Jr. and D. L. Jordan exposed Sprague-Dawley rats from a pathogen-free colony to Co⁶⁰ γ -rays of fission neutrons (see CRA 1(8):#1449, 1963). Almost all died with mammary tumors, but no histological examination is available. One can deduce that the relative biological effectiveness of the neutrons relative to γ -rays was 2 or perhaps more. R. Baserga, H. Lisco and W. E. Kisielewski showed that in rats subjected to a complex pattern of irradiation every 3 mo. (whole body, chest, right, then left kidney, whole body) there developed 4.6 tumors per rat (many malignant) in 100%, while there were 1.36 tumors per rat (mostly benign) in 55% of controls. This group also reported that tritiated thymidine (3HT; 1 or 10 $\mu\text{C/g}$) or Cl^{14} -thymidine (0.2 or 2 $\mu\text{C/g}$), given to newborn and young mice, increased tumor production after 22 and 18 mo., resp., as occurred in the offspring of female mice inj. with 250 μC of 3HT in the terminal wk. of pregnancy. The authors conclude that malignancy may result from radiation confined within multiple single cells. J. T. Duhig and M. Rifaat reported that AKR 3HT labeled leukemia lymphocytes induced leukemia earlier in all young mice compared to those receiving unlabeled cells. H. Cember and K. Stemme reported that intratracheally admin. $\text{Ce}^{144}\text{Cl}_3$ induced lung cancer in rats and apparently to a greater extent than insoluble $\text{Ce}^{144}\text{F}_3$ (see CRA 1(8):#1445, 1963).

- 63-1448 INGESTED ISOTOPES. (E.) Vaughan, J. (Med. Res. Coun., Bone-Seeking Isotopes Res. Unit, Churchill Hosp., Oxford, England). Pp. 462-481 in *Radiation Effects in Physics, Chemistry and Biology*. Proc. 2nd Internatl. Congress Radiat. Res., Harrogate, Gr. Britain, August 5-11, 1962. Ebert, M. and A. Howard (Eds.). North-Holland Publ. Co., Amsterdam, 510 pp., 1963.

A review is given of 19 papers presented at the congress that deal with various aspects of the effects and toxicity of ingested isotopes. Of special interest are many papers dealing with

the metabolism, histopathology and tumor formation due to radioactive isotopes which become localized in the bone. Several papers reported on the long-term experiment on isotope admin. to beagles (Utah experiment, work of T. F. Dougherty). After prolonged admin. of Pu²³⁹, W. S. S. Jee and B. J. Stover find that 95% of tumors arise from the spongy bone. In one dog the dose to the shaft of the humerus, based on terminal values of Pu²³⁹ per g wet bone was 2.2 K rad, compared with a max. of 15.6 K rad in the spongy bone. These values reflect the fact that tumors in the shaft require higher dose levels. (See also CRA 1(8):#1443, 1963.) J. I. Fabrikant and L. D. Smith who studied the effects of Pu²³⁹, Pu²⁴¹ and P³² in bones of the rat claim alpha radiation tends to produce sclerosing tumors while beta radiation gives rise to osteolytic lesions almost entirely. B. Q. Biskis and E. P. Finkel relative to their study of single or multiple inj. of Sr⁹⁰ in growing and mature dogs, state that no tumors originate directly from heavily damaged bone but in many instances they arise from fibrous tissue replacing the resorbed damaged bone.

63-1449 INCIDENCE OF MAMMARY NEOPLASMS IN NEUTRON- AND GAMMA-IRRADIATED FEMALE SPRAGUE-DAWLEY RATS. (E.) Vogel, H. H., Jr. and D. L. Jordan. Pp. 33-39 in Argonne National Laboratory. Biol. & Med. Res. Div. Semiannual Report, Jan. through June 1962. ANL 6723. Chicago & U. S. Atom. Energy Comm., 1963.

Animals employed were Sprague-Dawley rats obtained by Caesarean section and fostered by germ-free mothers; all were taken from litters born during the same week. First irradiation was carried out when rats were approx. 60 days old. A total of 57 rats in 4 groups were exposed to 1, 3, 6, and 35 rads/min. of fission neutrons (total 400 rads); 55 rats were exposed to comparable dose levels of Co⁶⁰ γ-rays (total 200 rads/wk. x 4). Of 112 irradiated rats, 92% had palpable mammary tumors after 600 days which were about equally divided between the 4 dose levels and which first appeared within 70 days after the first exposure. New tumors appeared continuously. The longest latent period was 99 days. Only 2 rats exposed to γ-rays and 7 exposed to neutrons died without palpable tumors. Neutron-irradiated rats died early, only 5 survived past 500 days, at which time there were still 23 alive in the γ-ray group.

63-1450 THYMIC TUMOR INCIDENCE AND LONGEVITY IN FEMALE MICE IRRADIATED WITH FISSION NEUTRONS OR Co⁶⁰ γ-RAYS. (E.) Vogel, H. H., Jr. and D. L. Jordan. Pp. 44-49 in Argonne National Laboratory. Biol. & Med. Res. Div. Semiannual Report, Jan. through June 1962. ANL 6723. Chicago & U. S. Atom. Energy Comm., 1963.

Groups of female CF No. 1 (Carworth Farms) mice, starting at approx. 100 days of age were irradiated with 100 rads/wk. x 4 of fission neutrons or with 200 rads/wk. x 4 of Co⁶⁰ γ-rays; 4 dose rates were employed, 1, 3, 6, and 35 rads/min. After 90-221 days after the last exposure, incidence of thymic tumors in the neutron group was 14/16, 11/13, 11/18, and 6/9, resp. (total 75%). In the γ-ray group incidence was 4/5, 6/7, 6/6 and 7/8, resp., (total 90%). Mean survival times of both neutron- and γ-irradiated mice were significantly shorter ($p = 0.02$) when the dose rate was 35 rads/min. than when it was 1 rad/min. This data plus the fact that thymic tumor was the chief cause of death would indirectly support the concept of a suggested relationship between leukemia incidence and dose rate of radiation.

63-1451 INDUCTION OF LEUKEMIA BY X-RAY IRRADIATION, ADMINISTRATION OF ESTROGEN AND THYMUS TRANSPLANTATION IN F₁ HYBRID MICE: A/JAX AND AKR CROSS. (E.) Nakakuki, K. (Dept. Path., Mie Prefectural U. Sch. Med., Tsu, Japan) and Y. Nishizuka. Acta Haemat. Jap. 25(6):786-792, 1962.

A total of 118 (A/Jax x AKR) F₁ hybrid virgin female mice, presumably carrying a leukemia agent, was divided into a control and 4 experimental groups and were observed from 6-24 mo. of age for evidence of leukemia. Incidence of leukemia among 24 (age 33-44 days) given whole body X-irradiation (150 r/wk. x 4) was 66.7%; among 19 given estradiol benzoate (20 μg/wk. x 20) incidence was 26.3%. When a portion of both the thymus and spleen of AKR mice (aged 26-40 days) were transplanted s.c. on opposite sides of the axillary region of 30 F₁ female mice of the same age, leukemia incidence was 26.7%. In a parallel experiment but one in which the donor mice were given whole body radiation (as already described) ending 1 wk. before transplantation, leukemia incidence was 26.7%. Leukemia incidence in 30 control mice was 6.7%. All of the leukemias in this experiment were of the lymphoid type.

63-1452 CARCINOMA OF THYROID IN CHILDREN: RELATION TO PREVIOUS IRRADIATION. (E.) Rachmaninoff, N. (Dept. Path., Harper Hosp., Detroit, Mich.). Harper Hosp. Bull. 21(5):166-171, 1963.

Seven cases of carcinoma of the thyroid are presented which were treated at Harper Hospital between 1949 and 1960. Two cases, a girl aged 9 and a boy aged 16 at time of admission, are described in detail because they had received prior irradiation for thymic enlargement at the age of 7 wk. and 5 yr., resp.

63-1453 A MODEL OF EXPERIMENTAL LUNG CANCER CAUSED BY INTRATRACHEAL INTRODUCTION

OF RADIOACTIVE CERIUM. (E.) Kurshakova, N. N. and A. E. Ivanov. Biull. Eksp. Biol. Med. (Eng.) 54(7):787-789, 1963.

A colloidal soln. of cerium¹⁴⁴ fluoride (particle size 25 mμ; dose 25 μC) was admin. intratracheally to rabbits by use of a syringe; they were then observed throughout their natural life. Tumors of the lungs were produced in 30% of 20 animals; they appeared between days 238-327 after admin. of the Ce¹⁴⁴. In 5 the tumors were bronchogenic and alveolar lung cancer, in one, non-cornifying squamous cell carcinoma of the esophagus. The minimum amount of energy absorbed by the lung tissue at the time of the first tumor (238 days) was equal to 51.4 k rad, and the max. (327 days) 68.9 k rad.

63-1454 SEQUELAE OF THE IRRADIATION OF C57BL MICE: HEPATOMAS. (Fr.) Méwissen, D. J. (Free U. Brussels, Belgium) and J. H. Rust. C.R. Soc. Biol. (Paris) 157(3):680-682, 1963.

Total gamma irradiation of C57BL mice causes the delayed appearance of hepatomas. The admin. of cystamine before irradiation does not appear to modify the carcinogenic action of the latter. It would appear as if hepatic oncogenesis is simply the result of a threshold dose.

63-1455 INDUCTION OF TUMORS IN RATS BY SUBCUTANEOUS IMPLANTS OF SURGICAL SPONGES. (E.) Dasler, W. (Dept. Biochem., Chicago Sch. Med., Ill.) and R. V. Milliser. Experientia 19(8):424-427, 1963.

Polyvinyl alcohol sponges implanted in animal tissues are less inactive than was generally assumed. Fibrosarcomas arose in 75% of the rats which survived at least 18 mo. after the s.c. implantation. (Author summary)

63-1456 INTRA-UTERINE IRRADIATION AND IRIS HETEROCHROMIA. (E.) Cheeseman, E. A. (Dept. Soc.

Prev. Med., Queen's U. Belfast, Scotland) and A. L. Walby. Ann. Hum. Genet. 27(Part 1):23-29, 1963.

The possible association between diagnostic X-rays in utero and the subsequent development of heterochromic sectors in the iris was investigated. Data were obtained relating to 97% (7813) of all school entrants aged 4-7 yr. to Belfast schools during 1961. Of these 67 (0.86%) were found to have heterochromic sectors of the iris. No significant (at $P = 0.05$) difference in the proportion affected was found between children reported by their mother to have been X-rayed in utero and others. In boys only, the prevalence of heterochromia was slightly, but not significantly, higher in those X-rayed in utero than in those not X-rayed. Eight affected boys were X-rayed in utero, and in as many as seven the X-ray occurred in the seventh month. This apparent conc., which was not observed in girls, is unlikely to be due to chance.

63-1457 RADIATION-INDUCED OSTEOGENIC SARCOMA IN PARABIONT RATS. (E.) Warren, S. (Cancer Res. Inst., New Engl. Deaconess Hosp., Boston, Mass.) and R. N. Chute. Lab. Invest. 12(11):1041-1045, 1963.

Parabiosis and shielding of one partner permitted the other to survive a supralethal single dose of 1000 r of whole body X-irradiation and to live to develop late complications. Parabiosis increased the incidence of osteogenic sarcoma in rats. Parabiosis and external whole body radiation produced osteogenic sarcomas, sometimes multiple, in about 5% of rats. Most osteogenic sarcomas produced were endosteal in origin. Osteogenic sarcomas varied widely in individually averaged increments of diameter, from 1.1 to 0.07 mm per day. Abnormalities of parathyroid glands were present but did not correlate with occurrence of osteogenic sarcomas. (Author summary)

See also abstract nos.: 1421, 1425, 1490

CHEMICAL CARCINOGENESIS

1458 CONVERSION OF ANTITUMOR INTO TUMOR PROMOTING EFFECT WITH PROLONGED INTAKE OF GRISOEFULVIN IN METHYLCHOLANTHRENE PAINTED MICE. (E.) Barich, L. L. (Jewish Hosp., Cincinnati, Ohio) and D. Barich. *Clin. Med.* 70(3):596, 1963.

Admin. of griseofulvin (GR; 10-15 mg/kg/day) to male Swiss mice, beginning either 2 wk. before or at the same time as treatment of the dorsal skin with a 0.5% soln. of 20-methylcholanthrene in acetone (2 drops on days 1, 5, 7, 11 and 13 and 15 on days 14, 18, 26, 32, 40 and 49), reduced the incidence of papillomas from a max. of 86.7% to a maxima of 16.7 and 41.7%, resp., for mice given GR 2 wk. before or at the start of carcinogenesis. The latent period for tumor development was also increased. Since previously published work had shown that pretreatment with the same dosage of GR for 6 wk. prior to 20-methylcholanthrene had a cocarcinogenic effect, increasing the number of tumors, while pretreatment for 4 wk. had no effect, the authors suggest that the antitumor effect of antimetabolic agents such as GR may be transformed into a tumor promoting effect after prolonged administration. Similar data from the literature regarding the probable cocarcinogenic effects of methotrexate, cyclophosphamide, arsenic, estrogens, urethane and a variety of alkylating agents are reviewed (36 references).

1459 BIOCHEMICAL AND MORPHOLOGICAL CHANGES IN RAT LIVERS DURING DIMETHYLAMINOAZOBENZENE-INDUCED CARCINOGENESIS AND THE ADMINISTRATION OF AMARANTH. (Rus.) Rubenchik, B. L. and A. I. Biukorez. *Vop. Onkol.* 9(4):68-74, 1963.

Feeding rats with dimethylaminoazobenzene (0.06% in the diet) for 18 wk. caused liver tumors and decreased activity of catalase and succinic dehydrogenase. Cathepsins at pH optimums of 3.5-5 increased in the early wk.; later the activity of the first decreased while that of the second increased. Liver riboflavin initially decreased and then returned to normal. In some experiments it was shown that there was a direct relation between the degree of morphological changes in the liver and the activity of catalase, succinic dehydrogenase and cathepsins. Prolonged feeding (40 wk.) with amaranth (0.2% in the diet) did not lead to any biochemical or morphological changes in the liver, nor did it induce tumors in other organs.

1460 HAIR CYCLE AND CHEMICALLY INDUCED EPIDERMAL CARCINOGENESIS IN MICE RECEIVING TRI-iodothyronine. I. FINDINGS AFTER SINGLE APPLICATION OF 9,10-DIMETHYL-1,2-BENZANTHRAcene. (E.) Sherwin-Weidenreich, R. (Dept. of Pathol., New York U. Sch. Med.) and F. Herrmann. *Invest. Derm.* 40(5):225-232, 1963.

The effect of L-triiodothyronine sodium (T_3 ; liothyronine) admin. on the hair cycle and on epidermal carcinogenesis was investigated in mice which received a single application of 9,10-dimethyl-1,2-benzanthracene (DMBA). Definite stimulation of hair growth was observed in all groups of animals which had received T_3 . No decrease in the tumor incidence was obtained under the influence of T_3 admin. In a group of male mice exposed to DMBA 2 wk. after completion of growth of 2nd generation hair, with T_3 started 1 wk. prior to carcinogen, 26% of 47 showed tumors, compared to 7% of 20 controls not given T_3 .

63-1461 SEXUAL DIFFERENCES IN EXCRETION OF o-AMINOAZOTOLUENE IN THE MOUSE. (Rus.) Belitskii, G. A. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci., Moscow). *Biull. Eksp. Biol. Med.* 55(5):96-100, 1963.

Following admin. of o-aminoazotoluene and diethylaminoazobenzene s.c. to mice of the CC57 and O20 strains, marked sexual differences were revealed in the urinary excretion of these preparations. Female excretion of free carcinogen and of diethylaminoazobenzene is nearly twice as high as in males. No sexual differences were revealed in excretion of trypan blue and indigocarmine.

63-1462 EFFECT OF SODIUM SALICYLATE ON TUMOR TRANSPLANTATION IN RATS. (E.) Stormby, N. G. (Inst. Path., U. Lund, Sweden). *Acta Path. Microbiol. Scand.* (Suppl. 163):76 pp, 1963.

Sodium salicylate (SS) treatment facilitated growth and survival of Ehrlich ascites cancer inoc. i.p. or intracutaneously into rats. It also produced a similar effect on the cancer inoc. intrarenally. The agent had no influence on transplants in the liver. The exudation of ascitic fluid and consequently the cancer growth were slightly inhibited during the first few days after transplantation (ascribed mainly to a salicylate-induced decreased capillary permeability), but this phase was followed by profuse and often fatal abdominal hemorrhage. Dissemination of cancer cells to lymph nodes seen in the salicylate-treated animals might also be due to an increased permeability of the vessel walls. In experiments with the Ehrlich mouse ascites cancer transplanted to hydrocortisone-treated rats growth was severely inhibited owing to decreased exudation and marked depression of stroma reaction in the host, although the survival of cancer cells was prolonged, probably by a reduced formation of antibodies. The take and growth of Rous rat sarcoma was also found to be facilitated by SS as well as by hydrocortisone, though the latter agent sometimes inhibited growth of the tumor. The homograft reaction was moderately depressed by salicylate, and then the tumor showed a stronger tendency to

infiltrative growth and lymphogenous spread. In rats, adrenalectomy was found to have no effect on the action of SS. This together with the apparently only slight effect of ACTH on tumor growth argues against the assumption that the effect of SS is transmitted exclusively via the hypophyseal-adrenal axis and for the assumption of specific properties of the drug.

- 63-1463 SUSCEPTIBILITY OF NEWBORN GERM-FREE MICE TO TUMOR INDUCTION BY 3-METHYLCHOLANTHRENE. (E.) Kelly, M. G. (NCI, Bethesda), W. L. Newton and R. W. O'Gara. Cancer Res. 23(7):978-982, 1963.

A single s.c. inj. of 0.1 or 0.3 mg of 20-methylcholanthrene (20-Me) in olive oil was admin. to newborn germ-free mice and to mice derived from the germ-free colony but reared under conventional conditions (CVN mice). The germ-free mice have no demonstrable infection with bacteria or fungi and no demonstrable antibodies to certain viruses commonly found in laboratory mice. There was little indication from the data that susceptibility to tumor induction by 20-Me was decreased by the absence of demonstrable infection with bacteria or by the apparent absence of certain murine viruses. In general, germ-free mice showed about the same susceptibility to induction of pulmonary tumors and s.c. sarcomas as did their conventional controls. Furthermore, leukemia was induced in a few of the germ-free animals but in none of the CVN mice. Females (germ-free and CVN) tended to be somewhat more susceptible than males to pulmonary tumor induction but only at the lower dose of 20-Me, 0.1 mg. (Author summary)

- 63-1464 EXPERIMENTAL INVESTIGATION ON THE CARCINOGENIC EFFECT OF IRON-DEXTRAN (URSOFERRAN). (Ger.) Kunz, J. (Inst. Path., Humboldt-U. Berlin), L. Shahab, K. Henze and H. David. Acta Biol. Med. German 10(5-6): 602-615, 1963.

The carcinogenic effect of a novel iron-dextran antianemic compound (ursoferran) was examined in rats by s.c. application. After a long latency period 55% of the rats treated by this compound developed rapidly growing polymorphocellular to spindle cell sarcomas at the site of inj. The tumor tissue could be cultivated in vitro and transplanted homologously in 8/30 cases. Control rats, to which iron-saccharate (vitaferri), dextran or NaCl solution had been inj., did not develop any tumors. Ways of the carcinogenic mode of action of iron-dextran are discussed in relation to its histochemically, chemically and electron microscopically proven conversion to siderin and ferritin. (Author summary)

- 63-1465 EXFOLIATIVE CYTOLOGY IN AN EXPERIMENTALLY INDUCED CARCINOMA OF THE HAMSTER

CHEEK POUCH. (E.) Stahl, S. S. (Murry Leonie Guggenheim Found., New York). Acta Cytol. (Phila) 7(4):262-267, 1963.

The medial wall of the left cheek pouch of male hamsters (av. wt. 36 g at start of experiment) received applications of 9,10-dimethyl-1,2-benzanthracene (0.5% soln. in oil) 3x/wk.; the animal were observed for periods up to 124 days. The evolution of the induced malignancy in the hamster cheek pouch was followed by clinical observation, cytologic smear and excisional biopsy. The developing tumor had a relatively short latent period which was accurately reflected in the cellular atypia seen in cellular specimens from the experimental site. A consistently high correlation was present between diagnoses derived from biopsy and cytologic study. (Author summary)

- 63-1466 STUDIES IN DIAGNOSIS IN ORAL SURGERY AND ORAL MEDICINE. CORRELATION OF CYTODIAGNOSIS AND BIOPSY IN THE EVOLUTION OF AN EXPERIMENTALLY INDUCED CARCINOMA. (E.) Stahl, S. S. (Murry Leonie Guggenheim Found., New York) Oral Surg. 16(8):985-993, 1963.

Further clinical, histologic and cytologic findings of the 9,10-dimethyl-1,2-benzanthracene-induced tumor in the hamster cheek pouch reported in CRA 1(8):#1465, 1963.

- 63-1467 SUCCESS IN CELL-FREE TRANSMISSION OF 20-METHYLCHOLANTHRENE-INDUCED RF MOUSE LEUKEMIA. (Jap.) Hiraki, K. (Dept. Int. Med., Okayama U. Sch. Med., Japan), S. Irino, T. Sezaki and M. Suzuki. Nippon Ketsueki Gakkai Zasshi (Acta Haemat. Jap.) 25(6):822-830, 1962.

The dorsal skin of 1-month-old RF mice was painted with 20-methylcholanthrene (20-Me; 5% in benzene 2x/wk.) for 4 mo. The incidence of leukemia was 88% (22/25), and of them 12 (48%) developed lymphoid leukemia and 10 (40%) myeloid leukemia. While attempts to inoc. cell-free filtrates from 20-Me-induced leukemic RF mice to newborn mice of the same strain were successful, the cell-free filtrate from mice with myeloid leukemia caused lymphoid leukemia in the recipients. This is suggestive of the possibility of transformation the type of leukemia during cell-free transmission. Intracerebral inoc. of cell-free filtrate from the brains of the leukemic mice also successfully produced leukemia in the inoc. mice. One mouse inoc. with a cell-free filtrate from the leukemic mice developed a mammary carcinoma. In the control group of mice not painted with 20-Me but inoc. with the filtrates prepared from normal RF mice, no leukemia or mammary carcinoma occurred. These facts suggest that the chemical carcinogen may act to induce leukemia by the "activation" of a latent virus resident in RF mice.

- 63-1468 EXPERIMENTAL AND CLINICAL STUDY ON MALIGNANT TUMOR (1st REPORT).

., Abstract) Hiraki, K. (Dept. Int. Med., Yamaguchi U. Sch. Med., Japan), S. Ofuji, T. Kadonami, I. Kimura, S. Irino, Z. Ota, T. Asano, K. Kageyama, K. Shinagawa, K. Okada, G. Ktsuka, I. Miyoshi, M. Kahara, T. Sezaka, R. Matsuura, T. Suchida, H. Kotani, K. Shibuya, T. Hiraoka, T. Imei, K. Ikejiri, M. Kunisada, U. Morinobu, T. Koriya, S. Suzuki, M. Sato, K. Takagi, H. Soda, T. Ama and M. Suzuki. Nippon Naika Gakkai Zasshi (Jap. Soc. Intern. Med.) 51(12):49-50, 1963.

Brief histological report is presented of the changes that occur in the induction of lymphoid myeloid leukemia in RF mice by 20-methylcholanthrene. In the preleukemic stage, hypoplasia was noted in the bone marrow and lymph nodes. (See also CRA 1(8):#1468, 1963.)

469 STUDIES ON CELL-FREE TRANSMISSION OF SPONTANEOUS AND 20-METHYLCHOLANTHRENE-INDUCED MURINE LEUKEMIAS. (E.) Okada, K. (Dept. Int. Med., Okayama U. Sch. Med., Japan), I. Miyoshi, M. Kunisada and M. Sato. Acta Haemat. Jap. 26(4):794-806, 1962.

Inducement of the leukemogenicity of AKR leukemia virus has been achieved by serial cell-to-cell passages through newborn AKR and Zb mice in which lymphoid leukemia was induced in 62.5% and 100% resp. In addition, the leukemia virus also induced leukemia in RF mice and AKR x C3H/He hybrids. In regard to AKR leukemia, females were more susceptible to the virus than males, and the incidence was observed between 4 and 5 mo. of age. In Zb mice leukemia susceptibility was reduced, and peak incidence fell between 5 and 6 mo. of age. The conc. of leukemia virus contained in the brain is less than that in liver, spleen, lymph nodes and thymus. A dominant hereditary trait is suggested as regards the transmission of susceptibility to the AKR leukemia virus. Newborn or suckling mice, less than 72 hr. old, were susceptible to the cell-free filtrates. Various physical and chemical studies indicate that the AKR leukemia virus is lipid-containing, medium sized virus of the RNA type. (See also CRA 1(8):#1467, 1963 for studies on 20-methylcholanthrene-induced leukemia.)

470 QUANTITATIVE STUDIES OF THE IMPORTANCE OF BENZOPYRENE FOR THE CARCINOGENIC EFFECT OF TOBACCO SMOKE. (Ger.) Druckrey, H. (Inst. Surg., Albert-Ludwigs-U., Freiburg, Germany), A. Schildbach. Zschr. Krebsforsch. 65(5):470, 1963.

In quantitative experiments on 120 rats, the minimal dose of benzpyrene (BP) was determined which would induce with weekly inj. the same number of sarcomas as tobacco tar (condensates of smoke) produced using the same technic. The minimal dose of BP varied between 300 and 660 µg. In contrast, the inj. amount of tobacco tar

(3.2 g) contained only 2.6 µg BP. Accordingly, only about 0.5% to at most 1% of the carcinogenic effect of tobacco tar could be explained by its content of BP. The total dose required to induce cancer did not increase with treatment with small individual doses given over a prolonged period, but instead became considerably smaller. On the basis of the results obtained the importance of BP for the carcinogenic effect of tobacco smoke is critically reviewed. (Author summary)

63-1471 3,4-BENZOPYRENE CONTENT OF SOVIET PARAFFINS. (Rus.) Prokhorova, E. K. (All-Union Res. Inst. Dairy Prod., Moscow) and N. N. Znamenskii. Vop. Onkol. 9(8):72-76, 1963.

Upon spectrofluorescent analysis, it was found that Grozno paraffin (brand A) and one of its oil fractions contained 3,4-benzpyrene (BP) as indicated by absorption at wavelengths 405-428 mµ and 390-435 mµ, resp. Novoufim and Soviet-made synthetic paraffin were also positive, with absorption at 390-435 mµ and 403-407.9 mµ, resp. BP content in Grozno paraffin was 2.6×10^{-3} µg/g. The BP content is believed to be related to a residue of oil.

63-1472 CROSS-REACTION BETWEEN BENZOPYRENE-INDUCED TUMOURS IN RATS AND MICE. (E.) Koldovsky, P. (Inst. Exp. Biol. Genet., Czech. Acad. Sci., Prague) and J. Svoboda. Folia Biol. (Praha) 9(3):233-236, 1963.

By means of preimmunization of A strain male mice with rat benzpyrene-induced tumors, with tumor XC induced in the same strain of rats by Rous sarcoma virus, Walker carcinoma and Yoshida sarcoma, it was found that benzpyrene-induced tumors in rats and mice possess at least a partially common tumor antigen. (Author summary)

63-1473 THE DUPLICATION OF DESOXYRIBONUCLEIC ACID AND EPIDERMAL CARCINOGENESIS. (E.) Ritchie, A. C. (Dept. Path., U. Toronto, Canada), J. V. Frei and H. Shinozuka. Acta Un. Int. Cancr. 19(3-4):579-581, 1963.

When papillomata are induced in mouse skin by a single application of a carcinogenic hydrocarbon (dimethylbenzanthracene) followed by repeated applications of croton oil, more papillomata appear if the carcinogen is given near midnight than if it is given near noon. The mitotic frequency in mouse epidermis is lower in the hours which follow midnight than in the hours which follow noon, but the frequency of epidermal cells synthesizing DNA is greater in the hours which follow midnight. It may be that in such experiments the carcinogen acts on cells synthesizing DNA. The admin. of orotic acid at the time the carcinogen was given did not alter the yield of papillomata. (Author summary)

63-1474 PHOTODYNAMIC ACTION AND CARCINOGENICITY
IN POLYCYCLIC HYDROCARBONS. (E.)

Santamaria, L. (Inst. Gen. Path., U. Milan, Italy).
Acta Un. Int. Cancr. 19(3-4):591-598, 1963.

The problem of the correlation between photodynamic action and carcinogenicity is studied employing 36 carcinogenic or noncarcinogenic polycyclic hydrocarbons and different tests. The photodynamic activity on blood serum is detected by a marked oxygen dependent alteration of the electrophoretic pattern, which is prevented by reducing agents. The polarographic analysis shows the rate of the photooxidation, which is of zero order or behaves in an exponential fashion. The photooxidation on isolated mitochondria is detected by a dramatic oxygen-dependent drop in turbidity which is not prevented by reducing agents. The correlation between photodynamic action and carcinogenicity is especially evident in the electrophoretic test (analysis of normal human blood serum photooxidized in the presence of a hydrocarbon).

63-1475 METABOLISM OF BENZO(a)PYRENE IN RATS
WITH AND WITHOUT LIVER INJURY. (E.)

Falk, H. L. (NCI, Bethesda). Acta Un. Int. Cancr. 19(3-4):528-530, 1963.

The metabolism of 3,4-benzpyrene and other polycyclic aromatic hydrocarbons in various rat strains is accomplished primarily in the hepatobiliary system by hydroxylation and conjugation of the parent compounds. Hepatic damage induced by CCl₄ results in qualitative and quantitative alterations in the metabolic profile, as determined by analyses of compounds present in the bile. A close correlation appears between biochemical alterations and histopathological abnormalities with restoration to normal occurring in both approximately simultaneously. (Author summary)

63-1476 INFLAMMATORY REACTIVITY AND CARCINOGENESIS. (E.) Salyamon, L. (Inst. Oncol., Acad. Med. Sci. USSR, Leningrad). Acta Un. Int. Cancr. 19(3-4):552-554, 1963.

Reactivity of rat and mouse liver tissue was reduced after *in vivo* treatment with hepatotropic carcinogens (CCl₄, p-dimethylaminoazobenzene, β-naphthylamine, 2-acetylaminofluorene). Degree of injury was determined on excised tissue by subjecting it to additional injury (heat) *in vitro* and measuring increase in swelling and increase in dye absorption. This inhibition of tissue response (so-called subaction) may be related to the process of malignant change and throws some light on the mechanism of cocarcinogenesis.

63-1477 ON SOME NEW ASPECTS OF EXPERIMENTAL
CARCINOGENESIS IN THYROID GLAND. (E.)
Napalkov, N. P. (Inst. Oncol., Acad. Med. Sci.

USSR, Leningrad). Acta Un. Int. Cancr. 19(3-4):756-758, 1963.

The data obtained in different experiments in rats treated with 6-methylthiouracil (MTU) and 3-amino-1,2,4-triazole showed that a distinct stepwise character is peculiar to the development of the precancerous changes and their onset is related to the alteration of the typical reaction of thyroid epithelial cells to the continuous admin. of goitrogens. The histogenesis of experimental squamous cell tumors is explained on the basis of the "metharysis" (methortosis) phenomenon. Combined treatment with goitrogens and androgens as well as repeated stress reactions accelerated the development of thyroid neoplasms while estrogens had an opposite action. The simultaneous inj. of CCl₄ prevented the hyperplasia of the thyroid but did not affect the tumor development in animals treated with MTU. In rats of several successive generations treated with MTU a change in the tumorous response was found. The experiments with aminotriazole indicate it is still necessary to remember the possible direct carcinogenic action of so-called antithyroid compounds. (Author summary)

63-1478 BENZENE LEUKEMIAS. (E.) Tareeff, E. (Acad. Med. Sci. USSR, Moscow), N. M. Kontchalovskaya and L. A. Zorina. Acta Un. Int. Cancr. 19(3-4):751-755, 1963.

Observations on 6 cases of acute and 6 of chronic leukemia confirm the possibility of the development of leukemia and related disorders of the hematopoietic system on the basis of long-term benzene poisoning (industrial exposures of 4-22 yr.). The development of acute leukemia most often originates against a so-called preleukemic state of hematopoiesis of the hypo- and aplastic forms. Chronic leukemia may possibly progress even without such a preleukemic state being detectable.

63-1479 THE RELATIONSHIP BETWEEN DOSE AND
CARCINOGENIC RESPONSE OBTAINED BY INJECTING METHYLCHOLANTHRENE INTO THE PERITONEAL CAVITY OF CHICKENS. (E.) Arthur, J. W. (Dept. Zool., Washington State U., Pullman) and H. L. Eastlick. Growth 27(3):199-204, 1963.

Sarcomas were observed in 14 out of 125 White Leghorn chickens inj. i.p. with five different conc. of 20-methylcholanthrene (MC) in sesame oil (total doses of 0.03, 0.3, 3.0, 6.0 and 9.0 mg). Since sarcomas were obtained only in chickens inj. with 3 or more mg of MC, a threshold or minimal dosage is required to elicit tumor formation in the strain of chickens used. Tumor incidences in the 3.0, 6.0 and 9.0 mg groups was 2/25, 2/25 and 10/25, resp.; av. latent periods (wk.) were 68.0, 53.0, and 47.3, resp.

1480 A NEW ANTIBIOTIC WITH CYTOSTATIC PROPERTIES: RUBIDOMYCIN. (Fr.)
ost, M. (Res. Lab. Soc. Chem. Factories,
ne-Poulenc, Vitry-sur-Seine, France), P. Ganter,
Maral, L. Ninet, S. Pinnert, J. Preud'homme
G.-H. Werner. C.R. Acad. Sci. (Paris)
(11):1813-1815, 1963.

part of a study of the new antibiotic rubido-
in, it was shown that the compound had a
ght carcinogenic effect, producing s.c. sar-
as at the site of inj. in some XVII mice.
idomycin had some teratogenic activity in 4-
old chicks, but not in GS or RP mice.

1481 TERATOGENIC ACTION OF BEE VENOM.
(E., Abstract) Ruch, J. V. and
Gabriel-Robez-Kremer. Excerpta Med. Sect.
0):163-165, 1963.

venom in the form of Apivene (which contains
active principles without the substances
t induce shock) was inj. into the albumen of
ck eggs in doses of 0.2-0.4 ml at the commence-
t of incubation or after one or two days of
ubation. Apivene diffuses very readily. The
ryos were examined on day 11. Among 378
s treated before incubation, mortality was
; of the living embryos 15% (14/93) were mon-
rs. Among 252 eggs treated on day 2 of in-
ation, mortality was 46%; and 9/135 of the
ing embryos (6%) were monsters. Among 410
s treated on day 3, mortality was 16%; of the
ing embryos 6% (21/341) were monsters. A
at number of the dead embryos showed mal-
mations. The serious malformations that
ally occur involve the nervous system, the
raco-abdominal wall, the beak and neck (crossed
partly absent beaks), and the posterior limbs
romelia, amyotrophia). In 29 of these mon-
rs, the heart showed marked malformations.
reat number of the treated embryos showed
y posterior micromelia.

1482 THE TERATOGENIC ACTION OF CORTISONE ON
THE HEART OF THE RABBIT. (E., Abstract)
vert, J., Y. Rumpler and J. V. Ruch. Excerpta
Sect. 1(70):31, 1963.

es of from 1 to 2 mg/kg of 9 α -fluoro-16 α -
hyl-delta-hydrocortisone 21-phosphate (dexa-
hasone 21-phosphate), inj. daily from the 11th
the 14th day of pregnancy, result in frequent
diac anomalies, such as partial or total
nesis of the interauricular, the interventric-
r, or the bulbar septa. A single dose of 8
may, if inj. on the 11th or 12th day of preg-
cy, produce similar lesions. It is concluded
t, in the rabbit, cortisone is strongly terato-
ic for the heart. (Author summary)

1483 CHANGES IN ULTRASTRUCTURES OF RAT LIVER
CELLS DURING AZO DYE CARCINOGENESIS.

III. CHANGES OF RAT LIVER CELLS IN PRECANCEROUS
STAGE OF 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE
FEEDING. (Jap.) Takahashi, G. (Dept. Path.,
Sapporo Med. Coll., Japan). Sapporo Igaku Zasshi
(Sapporo Med. J.) 23(1):1-19, 1963.

The liver of rats fed with 3'-methyl-dimethyl-
aminoazobenzene for 30 to 100 days were examined
with the light and electron microscope. Compact
aggregations of agranular endoplasmic reticulum
(ER) which was found by Suzuki, to be specific
for the carcinogen, were formed even in a very
early stage of the dye feeding, and was especially
pronounced as feeding was prolonged. This par-
ticular change of ER was more pronounced in cells
in the periportal area than those in other por-
tions of the liver lobule, and the cells with
profound alterations in ER seemed to undergo
ultimate condensation and destruction. In the
periportal areas of liver lobules, large hyper-
trophic liver cells were frequently found, and in
their cytoplasm the characteristic change of ER
was always seen. This finding suggests that these
hypertrophic cells also undergo degeneration and
destruction. On the other hand, proliferations of
small basophilic liver cells occurred in the
central area of the liver lobules, giving rise
later to a nodular hyperplasia; in each of these
hyperplastic foci, other centers of the cell pro-
liferation developed. A poor development of ER
in these small liver cells is regarded as an
evidence of their immaturity, and furthermore a
lack of the specific ER suggests that these cells
might be somehow resistant to the carcinogen. It
is suggested that the specific change of ER might
be a result of an interaction between ER of the
mature liver cells and the carcinogenic azo dyes.
The specialized function of the liver as a whole
is considered to be compensated by a continuous
proliferation of the liver cells. (Author summary)

63-1484 THE EFFECT OF ADENOSINE TRIPHOSPHATE
AND ITS DECOMPOSITION PRODUCTS ON CORTI-
SONE INDUCED TERATOLOGY. (E.) Gordon, H. W.
(Res. Dept., St. Barnabas Med. Ctr., Newark, N.J.),
W. Tkaczyk, L. A. Peer and W. G. Bernhard. J.
Embryol. Exp. Morph. 2(Part 3):475-482, 1963.

In an extension of previously reported work (see
CRA 1(5):#864, 1963), a study was made of the
effect of certain decomposition products of ATP
on the teratogenic effect of cortisone (C) on CFW
mice. In cortisone-treated groups, there was no
apparent effect of sodium pyrophosphate, adeno-
sine monophosphate (AMP), adenosine diphosphate,
and the related compound adenosine tetraphosphate
(Atetra P), on litter size. However, litter size
in similarly treated groups but without C were
larger. The experimental groups demonstrated a
pronounced increase in resorptions and deaths
compared to the control groups.

63-1485 CYTOSTATICALLY EFFECTIVE SULFONIUM
SALTS II. SULFONIUM SALTS WITH MONO-

AND DI-2-HALOGEN ETHYL RADICALS. (Ger.) Lüttringhaus, A. (Lab. Chem., Albert-Ludwigs U., Freiburg, Germany) and H. Machatzke. Arzneimittelforschung 13(5):366-370, 1963.

In a report on the synthesis of various sulfonium salts, of which some were cytostatic, one sulfonium salt, designated as Type D, a derivative of the hemi-sulfur mustards, was found to be wholly ineffective against Yoshida rat sarcoma, and partially carcinogenic.

63-1486 THE LACK OF EFFECT OF URETHAN (ETHYL CARBAMATE) ON SARCOMA INDUCTION BY THE SUBCUTANEOUS INJECTION OF 3,4-BENZOPYRENE. (E.) Berenblum, I. (Dept. Exp. Biol., Weizmann Inst. Sci., Rehovoth, Israel) and N. Trainin. Cancer Res. 23(7):983-986, 1963.

A total of 120 C57BL/6/JAX (C57) and 117 C3H/JAX (C3H) mice were given 3,4-benzpyrene (BP; 0.7 mg, s.c., right axilla); as additional treatment, 27 C57 and 29 C3H mice were given urethan (U; 30 mg, i.p.) 1 wk. prior to BP; 60 C57 and 55 C3H were admin. U (0.2 mg/wk. x 10, total 200 mg) starting 1 wk. after BP. The percentage with local sarcomas, the number of mice with sarcomas/number of mice alive when first sarcoma was seen, mean latent period (wk.), range of latent period (wk.), the number of survivors at 30 and 50 wk. were, resp.: C57 (BP alone): 24, 8/33, 26, 14-32, 25 and 22. C57 (U; 30 mg): 38, 10/26, 30, 22-62, 19 and 15. C57 (U; 200 mg): 32, 19/60, 33, 17-54, 39 and 37. C3H (BP alone): 55, 18/33, 32, 20-84, 21 and 16. C3H (U; 30 mg): 52, 15/29, 29, 20-49, 21 and 17. C3H (U; 200 mg): 55, 30/55, 29, 14-56, 36 and 21. U neither inhibited nor augmented the formation of local sarcomas. Lung adenomas occurred in most of the mice treated with multiple doses of U and occasionally in those treated with a single dose of U. Leukemia occurred in 8 mice: after 200 mg U, in 4/60 C57 and 3/55 C3H; after 30 mg U, in 1/26 C57. The action of U alone accounted for the development of lung adenomas and leukemia and appeared to be independent of the effect of prior s.c. inj. of BP.

63-1487 SELECTION FOR INCREASED SUSCEPTIBILITY TO INDUCED LUNG TUMOURS IN THE MOUSE. (E., Abstract) Bloom, J. L. (Inst. Anim. Genet., Edinburgh, Scotland). Acta Un. Int. Cancr. 19(3-4):797-798, 1963.

In an experiment, the aim of which was to increase the level of susceptibility to urethan, a strain of random-bred mouse was used which showed 49% resemblance (heritability) between parents and their offspring. From a previous experiment it was predicted that on the basis of selection, the level of susceptibility could be increased by about 2 tumors per generation. In the experiment in each generation the 15 pairs of parents with the highest mean scores were chosen and

four of their offspring, 2 males and 2 females, were treated with urethan and then used to produce the next generation. All matings were made at random among the selected litters, with the one limitation that matings of individuals with common grandparents were avoided. After 4 generations the mean tumor number increased from approx. 6 to about 13; response in unselected matings remained near the starting levels. (See also CRA 1(3):#439, 1963.)

63-1488 LIVER CANCER INDUCING EFFECT OF RECTALLY ADMINISTERED DIETHYLNITROSAMINE IN THE RAT. (Ger.) Schmähl, D. (Inst. Path., Rheinisch-Friedrich-Wilhelms-U., Bonn, Germany), C. Thomas and K. König. Zschr. Krebsforsch. 65(5):529-530, 1963.

The rectal admin. of diethylnitrosamine in rats in a daily dose of 3.2 mg/kg causes hepatocellular carcinoma but not local cancer. (Author summary)

63-1489 NEW EXPERIMENTAL DATA ON THE TUMOR INDUCING EFFECT OF ISONICOTINIC ACID HYDRAZIDE (INH). (Ger.) Juhász, J. (1st Inst. Path. Anat. Exp. Cancer Res., Medical U. Budapest, Hungary), J. Baló and B. Szende. Zschr. Krebsforsch. 65(5):434-438, 1963.

A total dose of 55 mg of isonicotinic acid hydrazide (isoniazid) in physiological saline was admin. to 50 albino mice i.p. for prolonged period. Between 95 to 400 days after start of treatment, various tumors developed in 15 animals (1 lung adenoma, 6 lymphosarcoma (mediastinal), 3 reticulum cell sarcoma, and 5 myeloid leukemia). In the control group there was only one instance of spontaneous leukemia. All medicaments which are admin. in large doses over a long period should be tested for their carcinogenic effects. (Author summary)

63-1490 COMPARATIVE STUDY OF SENSITIVITY OF NORMAL AND MALIGNANT CONNECTIVE TISSUE OF RATS TO THE ACTION OF CARCINOGENIC HYDROCARBONS (E.) Starikova, V. B. (Exp. Clin. Cancer Inst., Moscow) and Yu. M. Vasiliev. Acta Un. Int. Cancr. 19(3-4):620-623, 1963.

In *in vitro* cultures of 9,10-dimethyl-1,2-benzanthracene (DMBA)-induced and of cellophane-induced tumor cells, DMBA (2.5×10^{-1} mg/ml) inhibited mitotic rate, compared to controls. This conc. had no effect on Sarcoma 45 cells. Lower conc. (2.5×10^{-8} - 2.5×10^{-5}) inhibited mitosis of rat s.c. embryonic tissue, embryonic heart and granulation tissue (induced by cellophane implantation). Urethan (5 mg/ml) greatly increased the mitotic rate of DMBA-induced tumor cells but had no effect even at higher doses (10 mg/ml) on mitosis of Sarcoma 45 cells. At the higher conc. this latter drug inhibited mitosis of both rat s.c. embryonic tissue and of embryonic heart.

The results suggest that similar mechanisms are involved in DMBA and cellophane tumorigenesis.

63-1491 THE EARLY CHANGES INDUCED IN TISSUES BY CARCINOGENS. (E.) Laws, J. O. (Dept. Exp. Path., U. Leeds Sch. Med., England). *Acta Un. Int. Cancr.* 19(3-4):543-544, 1963.

Early changes occurring during carcinogenesis due to feeding with acetylaminofluorene were studied in Leeds albino rats, a strain which reacts slowly to the carcinogen. Partial hepatectomy performed between 3-7 wk. after commencing admin. reveals severe latent damage to the liver cells which fail to regenerate within the normal period. After a period of up to 10 days, if the animal survives, abnormal nodular regeneration sets in. Such livers explanted into tissue culture show rapid migration of isolated, irregular hepatic cells in place of the normal slow formation of sheets of cells. These changes are associated with changes in the adhesive properties of the cell surface. No definite changes have been demonstrated by the aniline-blue staining method, or the use of collagenase, which removes the surface material from liver cells, but studies using immunological techniques are in progress. (Author summary)

63-1492 AN ELECTRON MICROSCOPIC STUDY OF 20-METHYLCHOLANTHRENE-INDUCED DYSPLASIA OF THE UTERINE CERVIX. (E.) Scarpelli, D. G. (Dept. Path., Ohio State U., Columbus) and van Haam. *Acta Un. Int. Cancr.* 19(3-4):670-673, 1963.

Dysplasia of the uterine cervix of C3H mice, induced by 20-methylcholanthrene, was studied with the electron microscope. The earliest alterations of fine structure were evident in the cytoplasm of squamous epithelial cells. Round 155-435 m μ osmiophilic inclusions appeared within mitochondria of basal cells. The inclusions were bounded by double membranes resembling cristae. Cells containing many of these inclusions failed to show increased amounts of PAS, -SH or S-S positive material in their cytoplasm.

63-1493 DIFFUSION OF POLYBENZENE HYDROCARBONS IN THE LIVING ENVIRONMENT. (Fr.) Mallet, L. and L. Mallet. *Gaz. Hop.* 135(27):1142, 1963.

In a forest in Corrèze, 3,4-benzpyrene (BP) content (ng/100 g) of surface and deep samples of soil was 0.8 and 0.4, resp.; that of *Hypnum* moss (before and after hydrolysis), 0.35 and 4.6, resp.; content in a fungus (*Polyporus*) was 0.7. In Creuse, climbing ivy showed 8.5 μ g of BP in the branches and leaves but none in the fruit before hydrolysis whereas afterwards there was none in the branches and leaves but the fruits

showed a poly-condensed hydrocarbon with a spectrum approaching that of BP (4 μ g calculated as BP). BP content in the earth was 26. Mosses from the region of Eure-et-Loir had 1.90 μ g, in Auvers-sur-Oise, ivy leaves showed 0.75 and earth 2 μ g.

63-1494 TISSUE CULTURE STUDIES OF CELLS FROM MOUSE CERVIX SUBJECTED TO CARCINOGENIC TREATMENT. (E.) Fernandes, M. A. R. (Dept. Path., Hahnemann Med. Coll., Philadelphia, Pa.) and I. Koprowska. *Acta Cytol. (Phila.)* 7(4):215-223, 1963.

The uteri of groups of C3H/HE mice 4-6 wk. old were painted 2x/wk. with 3,4-benzpyrene (BP; 1% in acetone) for totals of 2-32 applications. Among 15 mice given 32 paintings, 3 clearly invasive carcinomas were produced. Among mice given 10-16 BP paintings, 2 microcarcinomas were noted among 11 observed 21-45 wk.; none were seen in 9 observed for 5-20 wk. In the group observed 21-45 wk., 2 carcinomas *in situ* developed among 13 given 2-16 paintings. A cell line (1732-33) developed from a pool of 2 uteri of mice subjected to 12 BP paintings and a line developed from a normal uterus both underwent an *in vitro* transformation from uniform to pleomorphic cultures.

63-1495 THE TUMOR-ENHANCING AND IRRITANT PRINCIPLES FROM *CROTON TIGLIUM* L. (E.) Van Duuren, B. L. (Inst. Industr. Med., New York U. Med. Ctr., N.Y.), E. Arroyo and L. Orris. *J. Med. Chem.* 6(5):616-617, 1963.

A more extensive report is presented on tumor-enhancing and irritant principles derived from a methyl alcohol extract of the seed of *C. tiglium* (see CRA 1(5):#855, 1963). The physical and some chemical characteristics are given for 4 components of an amorphous solid obtained by column chromatography of the methanol extract. Components A and C are irritant and show tumor-enhancing activity. When tested on female Swiss Millerton mice initiated with 9,10-dimethyl-1,2-benzanthracene (0.3 mg), compound C (5 μ g, 3x/wk.) induced tumors in 17/20 animals at 68 days; first tumors appeared at 44 days after initiation.

63-1496 PRECANCEROUS CHANGES IN THE ACTIVITY OF ENZYMES ASSOCIATED WITH TRYPTOPHAN METABOLISM AND THEIR RELEVANCY TO HEPATOCARCINOGENESIS. (E.) Kizer, D. E. (Samuel Roberts Noble Found., Inc., Ardmore, Okla.). *Ann. N.Y. Acad. Sci.* 103(2):1127-1136, 1963.

In transplanted rat and mouse hepatomas or primary hepatoma induced by 3'-methyl-dimethylaminoazobenzene (3'-MeDAB), the enzyme activity (reported as the percentage of the activity in control animals) of serotonin deaminase (SD), 5-hydroxytryptophan (5-HT) decarboxylase, tryptophan

pyrrolase (TP), and kynurenine hydroxylase (KH) underwent major deletion except for almost normal levels of SD with Morris rat Hepatoma 5123 (83%), and Mouse Hepatoma 134 (71%); 5-HT was also retained (140%) with Morris 5123. When 3'-MeDAB was fed to rats for 12 wk., neither SD nor TP appeared to undergo any appreciable change throughout the entire 12-wk. period so that further studies with a weak carcinogen 4'-MeDAB were not pursued. In groups of rats fed either compound there were decreases in 5-HT decarboxylase and KH activity. In groups of rats fed for 4 wk. with compounds of increasing carcinogenic potency (4'-MeDAB, 2'-MeDAB, DAB, 3'-MeDAB, 4'-F-DAB), there was correspondingly greater loss in activity of 5-HT decarboxylase and substrate induction of TP. Introduction of an ethionine block reduced both of these enzymes; however, combined feeding of ethionine plus methionine reduced the loss of 5-HT decarboxylase but resulted in greater loss of the other enzyme. Hypophysectomy had no appreciable effect on liver 5-HT decarboxylase activity in rats fed 3'-MeDAB; addition of growth hormone produced no significant further change. It appeared that none of the changes in the activity of any of the 4 enzymes was relevant to the process of hepatocarcinogenesis as induced by either azo dyes or ethionine.

63-1497 A HYPERNEPHROMA ASSOCIATED WITH ELEVATED LEVELS OF BLADDER CARCINOGENS IN THE URINE: CASE REPORT. (E.) Kerr, W. K. (Dept. Surg., Banting Inst., U. Toronto, Canada), M. Barkin, I. A. D. Todd and Z. Menczyk. *Brit. J. Urol.* 35(3):263-266, 1963.

A pt. with a constant filling defect of the left renal pelvis, after admin. of a loading dose of 100 mg/kg of tryptophan, showed in a 24-hr. urine collection about 40% carcinogenic metabolites (3-OH kynurenin plus 3-OH anthranilic acid); normal range is considered to be less than 10%. During simultaneous 15-min. differential ureteral collections, conc. of carcinogenic and non-carcinogenic metabolites from the right kidney were 5.0 and 121.0 µg/ml; for the left kidney, 12.0 and 195.0 µg/ml; resp., to give ratios for the right and left kidneys of 0.04 and 0.06, resp. Upon surgical exploration of the left kidney a very small tumor was found which proved to be a hypernephroma (Grade I adenocarcinoma).

63-1498 NAPHTHALENES IN CIGARETTE SMOKE. (E.) Johnstone, R. A. W. (Med. Res. Coun. Unit, U. Exeter, England) and P. M. Quan. *Nature (London)* 200:1184, 1963.

The isolation and identification of naphthalene, 2-methyl-, 1-methyl-, 2,7-dimethyl-, 2,6-dimethyl-, 1,6-dimethyl- and 1,3,6-trimethylnaphthalene in cigarette smoke is described. The positions of the methyl groups indicate terpenoid precursors of these naphthalenes, and an extension of the previously suggested mode of thermal decomposition

of isoprenoid polyolefines can account fully for the formation of polycyclic hydrocarbons in cigarette smoke.

63-1499 FORMATION OF INTRANUCLEAR INCLUSION BODIES IN TISSUE CULTURE CELLS BY 4-HYDROXYLAMINOQUINOLINE N-OXIDE. (E.) Endo, H. (Cancer Res. Inst., U. Kyushu, Fukuoka, Japan) and F. Kume. *Naturwissenschaften* 50(18):596-597, 1963.

When a monolayer of Chang's liver cells was incubated with an optimal conc. of 4-hydroxylaminoquinoline N-oxide (4-HAQO; 7×10^{-5} M) for 24 hr. intranuclear inclusion bodies (each surrounded by a halo) were noted which phenotypically appeared to be identical to those produced by the use of 4-nitroquinoline N-oxide (4-NQO). Since fibrosarcomas in rats have been induced by the s.c. inj. of 4-HAQO, these experimental results suggest that 4-HAQO might be the active intermediate in 4-NQO carcinogenesis.

63-1500 THE EFFECT OF PAINTING WITH CYCLICAL TERPENES ON THE SKIN OF WHITE MICE AND ON THE SKIN CARCINOMA DEVELOPED BY BENZYPRENE PAINTING. (E.) Benko, A. (1st Dept. Med., Szeged Med. U., Hungary), T. Tiboldi and J. Bardos. *Acta Un. Int. Cancr.* 19(3-4):786-788, 1963.

The effect of painting a mixture of essential oils (menthone, menthol, camphor, α - and β -pinenes, eucalyptol (cineol) and borneol) on mouse skin was determined as well as their influence on carcinoma induced by skin painting with 3,4-benzpyrene (BP). After 4.5-6.0 mo. of twice-weekly paintings with the terpenes alone, no carcinomas developed. When BP (0.5% in benzene-paraffin soln.) was similarly employed, incidence of carcinoma was 85%; incidence was 76% when the BP was dissolved in the terpene mixture. When the twice-weekly applications of BP were alternated (on different days) with twice-weekly paintings with the terpene mixture, carcinoma incidence was 33%. It is suggested that the terpenes might interfere with the carcinoma-inducing effect of BP because of structural relationships or through some interaction, with a possible change in its electron structure.

63-1501 EXPERIMENTAL INDUCTION OF SQUAMOUS CARCINOMA OF THE LUNG, OESOPHAGUS AND STOMACH. THE MODE OF THEIR INDUCTION. (E.) Schoental, R. (Toxic. Res. Unit., Med. Res. Coun. Lab., Carshalton, Surrey, England). *Acta Un. Int. Cancr.* 19(3-4):680-683, 1963.

After admin. to mice of diazomethane (DZM; 12 doses in 6 wk.), addition of oral 3,4-benzpyrene (BP; 1-2 mg x 2) 7 hr. after the last dose of DZM did not alter incidence of lung tumors compared to DZM only (5/5 and 5/5, resp., in 6 mo. survivors) but did induce 2 stomach tumors in addition. In similar groups of rats, the only tumors formed were of the lung and in the DZM + BP

2-4 mg x 1) group (3/5). In rats given monthly doses of N-methyl-N-nitrosourea (NMU; 1-2.5 mg x 3), incidence of lung and stomach tumors was 0/5 and 2/5, resp.; with addition 4 days after the last dose of BP (2 mg x 1, given 4 days after the last dose of NMU), tumor incidences were 0/4 and 2/4. In mice given NMU alone (0.25-0.50 mg x 2), lung and stomach tumors were found 1/5 and 2/5, resp.; with addition of 1 dose of BP (1 mg x 3), incidences were 2/10 and 7/10, resp.

1502 CANCER GROWTH ENHANCED BY STEROIDS. (E.) Kelly, M. (Inst. Rheum., Melbourne, Australia). Rheumatism 19(4):83-87, 1963.

A paper which is predominantly a review (70 references) of the enhancement of tumor growth by steroids, the author presents 3 previously unpublished cases. Massive intestinal metastases developed in 1 case 11 yr. after a resection when arthritis was inj. for bursitis. A pt. who chronically used cortisone drops in the eye, accidentally touched some beryllium to the area over which the soln. flowed. He then developed an anaplastic rhabdomyosarcoma of the soft tissues of this cheek. A woman, 47 yr. after a subtrochanteric amputation for osteogenic sarcoma, developed arthritis which was treated with cortisone. Within a few wk. she developed a lump in the breast which after excision proved to be a scirrhous carcinoma.

1503 CHLORPROPAMIDE AND FOETAL DAMAGE. (E.) Campbell, G. D. (King Edward VIII Hosp., Durban, Natal). Brit. Med. J. 1:59-60, 1963.

The previously published series is reviewed. Perinatal mortality in pts. on a daily dose of 500 mg chlorpropamide was 14 out of 19 pregnancies; 3 pregnancies in pts. on 250 mg/day there were no deaths. In a series on tolbutamide, perinatal mortality was 23% of 20 cases. Follow-up of one survivor revealed that the child was suffering from an advanced degree of microcephaly; the child was also suffering from a spastic quadriplegia. Experience with this last case reinforces the position that chlorpropamide should be withheld from pregnant insulin-dependent diabetics in favor of tolbutamide.

1504 HISTOPATHOLOGICAL STUDIES ON PULMONARY REACTION BY BERYLLIUM OXIDE IN RAT. EXPERIMENTAL TUMOROUS ACTION OF BeO COMBINED WITH CARCINOGENIC HYDROCARBONS. (E., Abstract) Udagawa, T. Bull. Tokyo Med. Dent. U. 9(3):440, 1963.

Albino rats (Saitama strain) received single intratracheal infusions of BeO (20 mg; B group); + 20-methylcholanthrene (emulsified, 3 mg; BM group); B + 3,4-benzpyrene (3 mg; BBp group). The group received carbon black (3 mg) + 3 mg of 20-methylcholanthrene (CM group). Highest frequency of lung tumors was in the BM group (10/40

observed from 1-6 mo.). There were no tumors in groups of 20 B and BBp rats but there was some metaplastic proliferation. In the CM group there was 1 tumor among 20 rats. Thus, the beryllium showed greater promoting action than carbon black.

63-1505 THE RESPONSES OF THE ALBINO RAT LUNG AGAINST CARCINOGENIC HYDROCARBON: A STUDY ON EXPERIMENTAL INDUCTION OF PULMONARY TUMOR. (E., Abstract) Udagawa, T. Bull. Tokyo Med. Dent. U. 9(3):413, 1963.

The albino rats (Saitama strain) were given single inj. of 3 mg of 20-methylcholanthrene, either adsorbed on carbon black or suspended in Tween-80 and water, by 3 different methods: direct, intratracheal and i.v. The histological changes of the lungs were followed for 120 days. In the lung parenchyma, several types of epithelial proliferation occurred in close relationship to the inj. material, which was indicated by the carbon particles in the former groups. In contrast, no mesenchymal tumors were observed. Lung cancer development was highest in frequency (7/22) in the group of rats which received direct intrapulmonary inj. of 20-methylcholanthrene adsorbed on carbon black. Incidence and intensity of epithelial hyperplasia was low in the groups in which the test material was introduced by the intratracheal or i.v. routes. The author recommends the transdiaphragmatic inj. as the method of choice in the study of experimental carcinogenesis of rat lung.

63-1506 EXPERIMENTAL STUDIES OF OCCUPATIONAL LUNG CANCER. (E., Abstract) Toda, M. Bull. Tokyo Med. Dent. U. 9(3):440, 1963.

Albino rats (about 400) were given a single intratracheal inj. of 20-methylcholanthrene combined with a dust suspension: Cr₂O₃ (CM group); NiO (NM group); Al₂O₃ (AM group); and SiO₂ (SM group). Incidence of neoplasms (all squamous carcinoma) during a period of observation of 1-6 mo. was 5/30 group NM, 3/40 group CM, 1/15 group SM and none in group AM. Incidence of hyperplastic proliferation was 12/30, 4/40, 2/15, and 1/15, resp. Crystalline 20-methylcholanthrene remained localized for as long as 6 mo. as determined by examination with UV.

63-1507 ENDOCRINOLOGICAL STUDIES OF THE DEVELOPMENT OF CARCINOMA OF THE UTERINE CERVIX. (Jap.) Koga, K. (Dept. Obstet. Gynec., Kyōshō U. Sch. Med., Japan), Y. Okamura and Y. Tanaka. Rinsho Fujinka Sanka (Clin. Gynec. Obstet.) 17(5):385-391, 1963.

Carcinogenesis due to 3,4-benzpyrene was studied on the uterine cervix of the mouse. Estradiol benzoate (used as a cocarcinogen) in a dosage of 0.01 mg inj. 2x/wk. (duration not stated) caused an acceleration of the carcinogenic effect.

Testosterone propionate (0.09 mg/wk., duration not stated) had the opposite effect. It is suggested that the high incidence of uterine cervical carcinoma in the human with dysfunctional ovaries could be due to the quantitative and dynamic imbalance of various hormones which act as cocarcinogens.

63-1508 EFFECTS OF CARCINOGENIC AMINES ON AMINO ACID INCORPORATED BY LIVER SYSTEMS. II. A MORPHOLOGICAL AND BIOCHEMICAL STUDY ON THE EFFECT OF DIMETHYLNITROSAMINE. (E.) Mukherjee, T. (Dept. Biophys., U. Stockholm, Sweden), R. G. Gustafsson, B. A. Arzelius and E. Arrhenius. *Cancer Res.* 23(6):944-953, 1963.

Comparative morphological and biochemical studies have been performed on liver from rats treated *in vivo* with dimethylnitrosamine (DMN; 20-100 mg/kg body wt. and in a time range of 2-20 hr.). A reduced capacity of mitochondria-free liver homogenates to incorporate labeled amino acids into proteins was confirmed with short-time *in vivo* treatments (2-3 hr.). Electron microscopy on liver tissue from the same animals revealed marked changes in the endoplasmic reticulum but no notable effects in other cellular structures. Prolongation of *in vivo* treatment to 20 hr. enhanced the inhibitory effect in the high dose range (100 mg/kg). These livers showed generalized damage of the liver cytoplasm and indications of necrobiosis. After treatment for 20 hr. *in vivo* with a low dose (20 mg/kg), on the other hand, a stimulation of the amino acid incorporation activity in cell-free systems was obtained, which masked the primary inhibition. The stimulatory effect was associated with an increase in the glycogen content. The structural changes, which have been considered to be reflected in this secondary stimulation of microsomal functions, were a marked swelling of the rough-surfaced endoplasmic reticulum, and great amounts of glycogen clusters appearing in the regions of the enlarged smooth endoplasmic reticulum. The secondary stimulation is interpreted as being mainly due to an increased sensitivity of the liver to glucocorticoids. (Author summary)

63-1509 A COMPARISON OF THE PATHOLOGICAL EFFECTS OF 2-ACETYLAMINOFLUORENE, 4-ACETYLAMINOBIPHENYL, AND 2-ACETYLAMINOBIPHENYL IN THE DOG. (E.) Jabara, A. G. (Dept. Path., U. Melbourne, Australia). *Cancer Res.* 23(6): 921-927, 1963.

The oral admin. of 2-acetylaminofluorene (2-AAF) to 7 bitches was followed by epithelial hyperplasia in the urinary bladders of 2 dogs surviving 40 mo., and one of these also developed multiple hepatomas. The oral admin. of 4-acetylaminobiphenyl (4-AAB) to 6 bitches induced metastasizing urinary bladder carcinomas in 3 dogs surviving 36 mo. or longer and multiple hepatomas in one of these animals. The oral

admin. of 2-AAB to 2 males and 6 bitches resulted in urinary bladder epithelial hyperplasia in one dog surviving 21 mo. of treatment, and dysplastic proliferation in the urinary bladders of 6 surviving 39-41 mo. 4-AAB was a more potent bladder carcinogen in the dog than 2-AAF but was not so active as its nonacetylated homolog, taking into account the dose levels and latent periods of the three amides. Hepatoma formation was not directly related to the amount of 2-AAF or 4-AAB consumed but appeared to depend mainly on the duration of admin. of amide and possibly partly on constitutional factors. Hepatomas induced with both 2-AAF and 4-AAB were histologically similar and resembled those arising spontaneously in dogs. The non-neoplastic hepatic changes induced with all 3 amides probably represented a nonspecific toxic reaction either to the compounds themselves or to their metabolites, rather than a precancerous state. (Author summary)

63-1510 THE EFFECT OF METABOLITES OF 2-NAPHTHYLAMINE AND THE MUTAGEN HYDROXYLAMINE ON THE THERMAL STABILITY OF DNA AND POLYRIBONUCLEOTIDES. (E.) Troll, W. (Inst. Indust. Med., New York U. Med. Ctr., N.Y.), S. Belman and E. Levine. *Cancer Res.* 23(6):841-847, 1963.

The mutagen hydroxylamine and the tissue carcinogens, 2-amino-1-naphthol and 1-amino-2-naphthol, lowered the transition midpoint (T_m) of salmon sperm DNA irreversibly and had similar effects on synthetic polyribonucleotides. The reaction appeared to be specific, since a number of metabolically related noncarcinogens had no effect on the T_m . The carcinogen 2-amino-1-naphthol was bound to the DNA in proportion to its ability to lower T_m , whereas chemically similar compounds without action on the T_m were not bound. The parallel action of a mutagen and carcinogen on DNA is of interest to the understanding of the mechanism of carcinogenesis. (Author summary)

63-1511 ZONAL ELECTROPHORESIS OF THE SOLUBLE PROTEINS OF LIVER AND TUMOR IN AZO DYE CARCINOGENESIS. (E.) Sorof, S. (Inst. Cancer Res., Philadelphia, Pa.), E. M. Young, M. M. McCue and P. L. Fetterman. *Cancer Res.* 23(6):864-882, 1963.

A procedure has been developed for the zonal electrophoretic resolution of the soluble proteins of rat liver with the use of a modified Porath column of ethanolyzed cellulose. An initial degree of resolution reproducibly separates the soluble liver proteins into all their principal charge classes with high recovery. The method has been applied to the separation of the soluble liver proteins of normal rats and those fed the strongly hepatocarcinogenic 3'-methyl-4-dimethyl-aminoazobenzene (3'-Me-DAB), the weakly carcinogenic 4'-methyl-DAB, the noncarcinogenic 2-methyl-DAB, or the control diet. The azoprotein profiles of whole extracts and their h subcomponents are

also presented. Azo metabolites are bound to the soluble liver proteins with a relatively high degree of specificity. The carcinogens produce more of the principal azoprotein (slow h_2) than does the noncarcinogen. The degree of electrophoretic homogeneity of this azoprotein matches those of certain species of individual enzymes, suggesting a single function for its normal protein analog. In addition to the slow h_2 , there exist two small families of soluble azoproteins, one of which appears to be ribonucleo-azoproteins in which dye is bound to the protein moiety, rather than to nucleic acid. Profiles of the soluble liver ribonucleoproteins are also presented, showing that they are localized in one electrophoretic class. The amount of the relatively basic (h) proteins, in particular the slow h_2 , is markedly reduced in 3'-Me-DAB-induced tumor compared with that of normal and azopre-neoplastic livers. In contrast to the pre-neoplastic liver, proteins of the tumor have no covalently bound azo dyes (Miller and Miller). In extension of that finding, the various soluble tumor proteins contain only very small quantities of loosely combined dyes. In particular, the small amount of h_2 proteins present has only a trace of such, if any. Finally, this report summarizes the various parallel involvements of the h_2 proteins of rat liver in hepatocarcinogenesis by aminoazo dyes and by 2-acetylaminofluorene, and of the h_2 -like proteins of mouse skin in skin carcinogenesis by polycyclic hydrocarbons. (Author summary)

63-1512 AUTOANTIGENIC NONSPECIFIC PROCESS IN RAT FED WITH DIMETHYLAMINOAZOBENZENE. (Fr.) Dufour, D. (Dept. Biochem., Fac. Med., J. Laval, Quebec) and J.-M. Boucher. Experientia 9(8):432, 1963.

This result reports the appearance of a non-specific autoantigenic process between the liver, the spleen and the serum of rats fed on a dimethylaminoazobenzene and diethylaminoazobenzene-containing diet. See also CRA 1(3):#444, 1963. (Author summary)

63-1513 POLYPOIDY AND ENDOREDUPPLICATION IN HUMAN LEUKOCYTE CULTURES TREATED WITH β -MERCAPTOPYRUVATE. (E.) Jackson, J. F. (Inst. Med. Genet., U. Uppsala, Sweden) and K. Lindahl-Lessling. Science 141:424-426, 1963.

Treatment of cultured human peripheral blood leukocytes with β -mercaptopyruvate resulted in marked increases in polyploidy and endoreduplication in squash preparations of mitoses in the metaphase stage. Since β -mercaptopyruvate occurs in man as an intermediary metabolite in cysteine degradation, it might contribute to the development of polyploidy *in vivo*, especially in tumors lacking desulfurase enzymes. (Author summary)

63-1514 TERATOGENIC EFFECT OF 5-HYDROXYTRYPTAMINE IN MICE. (E.) Poulson, E. (Dept. Pharm., Guy's Hosp. Sch. Med., London, S.E. 1), J. M. Robson and F. M. Sullivan. Science 141:717-718, 1963.

The s.c. inj. of a single dose of 5-hydroxytryptamine into pregnant mice produced a large number of fetal abnormalities, mostly of the eyes, limbs, and tail; the skull and central nervous system were also sometimes affected. These effects could result from the action of the drug on placental function and blood supply.

63-1515 CONGENITAL MALFORMATIONS IN HAMSTER EMBRYOS AFTER TREATMENT WITH VINBLASTINE AND VINCRISTINE. (E.) Ferm, V. H. (Dept. Path., Dartmouth Sch. Med., Hanover, N.H.). Science 141:426, 1963.

Intravenous inj. of vinblastine or vincristine, two antitumor chemotherapeutic agents used in humans, into pregnant golden hamsters on the 8th day of gestation causes an increase in the fetal mortality rate and the appearance of a significant number of congenital malformations in the surviving fetuses. (Author summary)

63-1516 THE ACTIVITY OF COLCHICINE ON THE PERITONEAL MESOTHELIUM OF THE WHITE RAT. (Rum.) Brătianu, S. (Inst. Med., Iasi, Rumania), L. Gavrilă, T. Onofrei and G. Dobrescu. Stud. Cercet. Med. Intern. 4(3):393-394, 1963.

As a starting point for their researches, the authors considered the hypothesis that cells with mitosis arrested in the metaphase are capable of resuming their mitotic activity in an atypical manner, if subjected to a mitosis-stimulating action and that the number of amitoses is increased by the alteration of the spindle system. The object of this work is to demonstrate that with this mechanism it is possible to obtain cells with a pseudocancerous appearance and an increase in the number of amitoses by using very small doses of colchicine, even without the presence of carcinogenic substances.

63-1517 CARCINOMA OF RAT LUNG FROM INTRAPLEURAL METHYLCHOLANTHRENE. (E.) Brown, C. E. (Lankenau Hosp., Philadelphia, Pa.). Arch. Path. 76(3):347-353, 1963.

A simple and effective method of inj. 20-methylcholanthrene-impregnated strings into the pleural cavity of 12 white Wistar rats produced squamous carcinomas of the lung in nine and bronchial adenomas in one. (Author summary)

63-1518 ELECTRON MICROSCOPY OF THE CYTOPLASM OF PARENCHYMAL LIVER CELLS IN α -NAPHTHYLISOTHIOCYANATE-INDUCED CIRRHOSIS. (E.) Steiner, J. W.

(Dept. Path., Banting Inst., U. Toronto, Ontario) and C. M. Baglio. Lab. Invest. 12(8):765-790, 1963.

Wistar rats fed an adequate diet supplemented with 0.1% α -naphthylisothiocyanate (ANIT) develop liver lesions characterized by a massive ductular cell reaction which leads to widespread disorganization of the parenchyma. Electron microscopy shows profound alterations of the electron-scattering potential of the nuclear and cytoplasmic matrix of entire liver cells, so that "light" and "dark" cells can be distinguished. The ergastoplasm of the liver cells becomes disorganized and ribosomes are lost from focal areas of the ergastoplasmic membranes. These and other changes are very similar to the alterations produced in liver cells by the admin. of certain hepatic carcinogens. Since ANIT is not carcinogenic when admin. in the manner employed, the conclusion was reached that these alterations cannot be interpreted as indicative of a preneoplastic modulation of liver cell organelles. (Author summary)

63-1519 STUDIES ON THE NEWT TEST FOR CARCINOGENICITY. 3. NON-CARCINOGENIC AND WEAK CARCINOGENIC HYDROCARBONS. (E.) Arffmann, E. (Dept. Path., Finsen Inst., Copenhagen). Acta Path. Microbiol. Scand. 57(4):375-394, 1963.

Some noncarcinogenic and weak carcinogenic hydrocarbons have been tested on Triton cristatus. Phenanthrene and, with a few exceptions, anthracene and triphenylene gave no epithelial response, while chrysene and benz[a]anthracene induced a positive reaction, estimated as weak or moderate according to the incidence. In disagreement with reviewed results in mammals was the negative reaction to 1,2,4-trimethylphenanthrene and the positive response to 3',6-dimethyl benz[a]anthracene. The results, including some quantitative experiments, are discussed, and it is preliminarily concluded that the newt test has shown sufficient specificity to be used as a quick test for carcinogenicity, at least of polycyclic hydrocarbons. (Author summary)

63-1520 BIOASSAYS ON THE CARCINOGENICITY OF TOBACCO SMOKE CONDENSATES AND AIR POLLUTANTS. (E., Abstract) Wynder, E. L. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.) and D. Hoffmann. Proc. Am. Assn. Cancer Res. 4(1):73, 1963.

Studies with four tobacco types showed quantitative differences of their smoke contents in phenols and polynuclear hydrocarbons as well as in tumor potencies to mouse skin. After 12 mo. smoke condensates of Virginia cigarettes induced 30%, Turkish 22%, Maryland 10% and Burley 8% tumors. The tumor potencies of tobacco smoke condensates seem to depend on their benzo(a)pyrene and phenol contents. Certain terpenes also affect the activities of tobacco smoke condensates.

The diterpene allo-ocimene is a promoter in 1.0, 2.5 and 5.0% conc. on mouse skin initiated with 300 μ g 9,10-dimethyl-1,2-benzanthracene. After 8 wk. 30%, 40%, 47%, resp., tumor bearing mice were observed. Cigarette smoke contains up to 0.5% allo-ocimene. Bioassays for the carcinogenicity of the organic matter of air pollutants concerned, in particular, aromatic polynuclear hydrocarbons. The molar ratios of carcinogenic to weak or non-carcinogenic hydrocarbons are of importance. For the first group benzo(a)pyrene was chosen; for the second benzo(e)pyrene, benz(a)anthracene, pyrene, fluoranthene, triphenylene and phenanthrene. Results show tumor promotion in one setting and tumor inhibition in another. Three dibenzopyrenes found in air pollutants, the other 3 known dibenzopyrenes and benzo(ghi)perylene and indeno(1,2,3-dc)pyrene were tested on mouse skin. (Author summary)

63-1521 THE TERATOGENIC EFFECT OF N-DESACETYLTHIOLCHICINE WITH OR WITHOUT THYROXIN. (Fr.) Faucounau, N. (Lab. Biol., Fac. Med., Bordeaux, France), R. Stoll and R. Maraud. C.R. Soc. Biol. (Paris) 157(4):780-782, 1963.

N-Desacetylthiocolchicine (Thiocolciran), an antimitotic poison, is teratogenic for the chick embryo. This effect is promoted by thyroxin, a substance which is not in itself teratogenic. This synergistic effect may be either quantitative, as has been shown with Thiocolciran, or both quantitative and qualitative, as has been previously shown with E-39, where the addition of thyroxin causes the appearance of new teratologic types. This effect of thyroxin with regard to phenotypic malformations suggests the intervention of epigenetic factors which influence "expressivity and penetrance" of malformations of a genetic origin. (Author summary)

63-1522 DEMONSTRATION OF FLUORESCENT HISTIOCYTES IN THE EXPECTORATION OF SMOKERS. (It.) Marmont, A. (Gen. Med. Clin., U. Genoa, Italy), E. Damasio and A. C. Negrini. Acad. Med. 1-2(77):86-90, 1963.

The analysis of the expectoration of smokers by fluorescent microscopy revealed the presence of cells of the histiocyte type (pulmonary or alveolar histiocytes) which appeared to be strongly fluorescent. The phenomenon seemed to be due to the presence in these cells of polycyclic hydrocarbons and in particular to 3,4-benzpyrene. The origin of histiocytes, the nature of the fluorescent substances, and their possible bearing on oncogenesis are also discussed. (Author summary)

63-1523 TOBACCO SMOKING. SOME FACTORS WHICH MAY BE OF SIGNIFICANCE FOR THE CARCINOGENIC EFFECT OF POLYCYCLIC HYDROCARBONS. (Dan.) Lam, J. (Inst. Chem., Aarhus U., Denmark). Ugeskr. Laeg. 125(31):1064-1067, 1963.

By pyrolysis of constituents isolated from tobacco it is stated that a series of organic compounds can be converted into polynuclear hydrocarbons. The absolute and the relative amounts of these hydrocarbons vary with the temperature, mainly increasing with increasing temperature, within the range prevailing for cigarettes. As to the carcinogenic activity, promoting compounds may be acids or bases, the aromatic hydrocarbons being "dissolved" colloiddally in the presence of many organic acids and bases. The colloidal form of the hydrocarbons may facilitate the uptake in the living organism. (Author summary)

63-1524 INFLUENCE OF p-DIMETHYLAMINOAZOBENZENE (DAB) AND OF THE DEFICIENCY OF FLAVIN AND PROTEIN ON THE REACTION OF DETOXICATION FROM THE CARCINOGEN BY THE RAT LIVER. (Fr.) Emanoil-Ravicovitch, R. (Lab. Chem. Biol., Inst. Biol. Phys. Chem., Paris) and C. Hérisson-Cavet. Bull. Soc. Chim. Biol. (Paris) 45(5-6):613-621, 1963.

The respective effects of flavin and protein deficiencies and of carcinogen (DAB) on the DAB detoxication activity of rat liver during pre-cancerization were studied. The decrease of activity is directly dependent on the flavin and protein deficiencies. The carcinogen itself mainly provokes the decrease of the apoenzyme in the detoxication system. As far as the marked decrease in enzymatic activity is concerned the effect of flavin and protein deficiency on one hand, and the effect of the carcinogen on the other, are additive. (Author summary)

63-1525 THE EFFECT OF AGE, SEX, STRAIN, SPECIES AND DOSE LEVEL DIFFERENCES UPON THE METABOLISM OF 2-NAPHTHYLAMINE IN RODENTS. (E.) Dewhurst, F. (Mt. Vernon Hosp., Northwood, Middlesex, England). Brit. J. Cancer 17(2):365-370, 1963.

The percentage conversion of 2-naphthylamine to 2-amino-1-naphthol and its conjugates has been studied in a number of species of rodent including one (the guinea pig) not previously studied. Statistically significant sex differences in the metabolism of 2-naphthylamine were observed in the case of rats only. Young animals appear to convert a smaller percentage of a dose of 2-naphthylamine to 2-amino-1-naphthol conjugates than do adults. Well defined strain differences were observed in the case of mice. Dose level appeared to have no effect upon the percentage conversion. (Author summary)

63-1526 THE ATTEMPTED IN VIVO INHIBITION OF THE ORTHO-HYDROXYLATION OF 2-NAPHTHYLAMINE. (E.) Dewhurst, F. (Mt. Vernon Hosp., Northwood, Middlesex, England). Brit. J. Cancer 17(2):371-376, 1963.

The effects of a number of potential inhibitors upon the ortho-hydroxylation of 2-naphthylamine have been studied. Significant inhibition of the excretion of 2-amino-1-naphthol and its conjugates was observed with SKF-525-A (diethylaminoethyl diphenylpropylacetate), chlorpromazine and Dummy Beflavir (riboflavin preparation). No inhibition was observed with riboflavin, ascorbic acid, nicotinamide, pyridoxine HCl, 2,4-dinitrophenol, aspirin, or codeine phosphate. No significant stimulation of excretion was observed with any of the compounds. (Author summary)

63-1527 EARLY STAGE IN THE METABOLISM OF AMINO-AZO DYES IN THE LIVER OF RATS. (E.) Dijkstra, J. (Natl. Chem. Res. Lab., S. African Council Sci. Indust. Res., Pretoria). Brit. J. Cancer 17(2):355-359, 1963.

Shortly after intragastric admin. of a single dose of the carcinogen 3'-methyl-dimethylaminoazobenzene (3'-MeDAB) and of the noncarcinogen 2-MeDAB, and before binding of these dyes to proteins occurred, the trichloroacetic acid extracts of the liver of rats contained an azo dye, which differed from the dye admin. and from known metabolites in that it was not extractable from its aqueous soln. with ether or an acetone-benzene mixture. The conc. of this new metabolite was maximal at 5-6 hr. after dye admin. and declined to low values by 10 hr. In contrast, no formation of trichloroacetic acid-soluble dye was observed after admin. of the noncarcinogenic 4-aminoazobenzene, which is weakly bound to proteins. The possibility that the acid-soluble dye represents an early stage in the binding of aminoazo dyes to proteins has been discussed. (Author summary)

63-1528 STUDIES ON 1,2:5,6-DIBENZANTHRACENE-INDUCED MAMMARY CARCINOGENESIS IN MICE. (E.) Ranadive, K. J. (Indian Cancer Res. Ctr., Parel, Bombay, India) and K. A. Karande. Brit. J. Cancer 17(2):272-280, 1963.

In an attempt to study mechanism of mammary carcinogenesis induced by 1,2,5,6-dibenzanthracene (DBA), the carcinogen was admin. to 5 inbred strains of mice by 3 different routes: (1) cutaneous application, (2) s.c. implantation of pellets and (3) ovary painting. On cutaneous application of DBA significant acceleration of breast tumor incidence was observed in virgins and breeders of susceptible strains C3H(Jax) and dba(-MTI) and the breeders of strain L(P). On implantation of pellets, mammary tumors were induced in strains C3H(Jax), dba(-MTI), L(P) as well as strain Strong A. C57(Black) failed to develop chemically induced tumors in both the experiments. Ovarian histology showed certain changes. The ovary painted C3H and dba(-MTI) mice indicated some effect on the ovarian and uterine tissue, but there was no effect on the mammary tumor incidence. DBA-induced mammary

carcinogenesis data on five strains are compared with that of previously described MCA (20-methyl-cholanthrene?)-induced carcinogenesis and the mechanism is discussed in the light of the relevant literature. (Author summary)

- 63-1529 THE EFFECTS OF 1-(2-DIMETHYLAMINO-ETHYL)-2-PHENYLINDENE ON FIBROCYTES CULTIVATED *IN VITRO*. (E.) Powell, A. K. (Mt. Vernon Hosp., Northwood, Middlesex, England). *Brit. J. Cancer* 17(2):298-303, 1963.

Normal mouse embryo fibrocytes and sarcoma cells cultivated *in vitro* were treated continuously with 1-(2-dimethylaminoethyl)-2-phenylindene. All treated cells were rapidly killed by this drug at conc. of M/250 and M/1000. Concentrations of M/5000, M/25,000 and M/100,000 were slowly toxic. Fibrocytes were more resistant than sarcoma cells to the cytotoxic action of the drug. Normal fibrocytes exposed to the lowest drug conc. gave an unusual response, not shown by sarcoma cells, before they degenerated. Ex-plant cells changed to resemble ascites tumor cells and outgrowth fibrocytes simulated sarcoma cells on the coagula. (Author summary)

- 63-1530 TESTS FOR CARCINOGENESIS USING NEWBORN MICE: 1,2-BENZANTHRACENE, 2-NAPHTHYLAMINE, 2-NAPHTHYLHYDROXYLAMINE AND ETHYL METHANE SULFONATE. (E.) Roe, F. J. C. (Roy. Cancer Hosp., London, S.W.3), B. C. V. Mitchley and M. Walters. *Brit. J. Cancer* 17(2):255-260, 1963.

Groups of mice of the BALB/c (Bittner agent free) strain were inj. when newborn with the following test substances: 50 µg 1,2-benzanthracene (BA) and 50 µg 2-naphthylamine (NA) in aqueous gelatine, 100 µg ethyl methane sulfonate (EMS) in distilled water and 50 µg 2-naphthylhydroxylamine (NHA) in arachis oil. Solvent controls were inj. with 1% aqueous gelatine alone and arachis oil alone and a positive control group received 30 µg 9,10-dimethyl-1,2-benzanthracene (DMBA) in aqueous gelatine. A further control group received no treatment. Survivors were killed between the 36th and 43rd wk. of the experiment and examined post mortem for tumors at all sites. The incidence of lung and other tumors was high in the DMBA treated group--and low in the untreated and solvent treated control groups. According to these standards BA and EMS gave weak but definitely positive results and NA and NHA doubtful but probably positive results. When the same dose of BA (i.e., 50 µg) was inj. into mice of less than 24 hr., 24-48 hr., 4 days and 8 days of age, the highest yield of tumors was obtained in the first group. (Author summary)

- 63-1531 THE EFFECT OF PHENANTHRENE ON TUMOUR INDUCTION BY 3,4-BENZOPYRENE ADMINISTERED TO NEWLY BORN MICE. (E.) Grant, G.

(Chester Beatty Res. Inst., Roy. Cancer. Hosp., London, S.W.3) and F. J. C. Roe. *Brit. J. Cancer* 17(2):261-265, 1963.

Groups of newly born mice, less than 24 hr. old, were given suspensions of the following in 1% aqueous gelatin: 20 µg 3,4-benzpyrene (BP); 20 µg BP + 20 µg phenanthrene (PH); 40 µg BP; 40 µg BP + 40 µg PH; or 40 µg PH, and then kept for 52 or 62 wk. before they were killed. In addition two groups were observed following inj. of aqueous gelatin only. The incidence of pulmonary adenomas and of other tumors (lymphomas, hepatomas and mammary adenocarcinomas) seen in response to treatment with BP was not increased or reduced by the admin. of PH. The incidence of tumors in the group which received PH only was no higher than that seen in the two solvent-only control groups. (Author summary)

- 63-1532 STUDIES ON THE CARCINOGENICITY OF TRICYCLOQUINAZOLINE: THE EFFECT OF STRUCTURAL MODIFICATION. (E.) Baldwin, R. W. (Cancer Res. Lab., U. Nottingham, England), G. J. Cunningham, A. T. Davey, M. W. Partridge and H. J. Vipond. *Brit. J. Cancer* 17(2):266-271, 1963.

Modification of the arrangement of the homocyclic and heterocyclic rings of tricycloquinazoline (TCQ) results in almost complete loss of carcinogenic activity. These findings thus indicate that the overall molecular shape and size of TCQ are important for carcinogenicity. This hypothesis is further supported by the finding of tumorigenic activity with a hexacyclic compound which has a molecular shape intermediate between that of TCQ and the inactive isomer, iso-TCQ. No simpler azapolycyclic compound related to TCQ has been found to have significant carcinogenic activity, further supporting the concept that the overall molecular shape of TCQ is critical for carcinogenicity. The inactivity of quinazoline and 4-hydroxyquinazoline, two possible metabolites of TCQ, provides corroborative evidence. The implications of these findings to the mechanism of interaction of TCQ with cell receptors are discussed. (Author summary)

- 63-1533 MOUSE-SKIN PAINTING WITH SMOKE CONDENSATES FROM CIGARETTES MADE OF PIPE, CIGAR, AND CIGARETTE TOBACCOS. (E.) Homburger, F. (Bio-Res. Inst., Cambridge, Mass.), A. Treger and J. R. Baker. *J. Nat. Cancer Inst.* 31(6):1445-1459, 1963.

Groups of CAF₁ mice of both sexes were subjected to skin painting throughout their lifetime with acetone, benzo[a]pyrene, and smoke condensates. To make the condensates, tobaccos customarily used for manufacture of cigars, pipe mixtures, and cigarettes were smoked in the form of cigarettes. Combustion temperatures were practically the same for all types of tobaccos. The LD50 of

se condensates was lower for males than females, and lower for pipe smoke condensate than the other two. Except for the greater toxicity of the pipe smoke condensate manifested by water weight loss and mortality, there were no differences in the systemic effects of the condensates. No difference in organ weights ascribable to the treatment was found, nor were pathologic changes observed in vital organs except some papillary nephritis and skin lesions. Condensates caused skin papillomas and up to 23% epidermoid cancers, with slightly more cancers in females than in males. The rate of maturation of these lesions was slower with cigarette smoke condensate than with the two other condensates. The acetone controls showed no pathologic changes and only a low incidence of epidermal hyperplasia at the site of painting.

1534 MORPHOLOGIC AND BIOLOGIC CORRELATION OF LESIONS OBTAINED IN HEPATIC CARCINOGENESIS IN A X C RATS GIVEN 0.025 PERCENT N-FLUORENYLDIACETAMIDE. (E.) Reuber, M. D. (Dept. Path., Harvard Sch. Med., Boston, Mass.) H. I. Firminger. J. Nat. Cancer Inst. 31(6): 7-1429, 1963.

High correlation was found between the morphological interpretation and biological behavior of hepatic lesions induced by carcinogen feeding in rats. Inbred A X C male or female rats were fed 0.025% N-2-fluorenyldiacetamide in a semisynthetic diet for 2, 2.5, 3, and 4 mo.; laparotomy, liver biopsy, and transplantation were performed every 6-8 wk. Autologous and isologous transplants of normal and cirrhotic liver tissue, areas and nodules of hyperplasia (with a single exception) did not grow. A few "small hepatomas," morphologically comparable to "carcinoma *in situ*" and measuring 5 mm or less in diameter, also failed to grow. Hepatomas that measured a minimum of 7-9 mm in diameter. Most all primary hepatomas 1 cm or more in diameter grew autologously and isologously in transplant. Such well-developed hepatomas occurred only in animals given carcinogen for 3-4 mo. To determine the transplantability the animals with transplants were followed for a period of mo. The time of appearance of palpable growth, the rate of growth of the trans-

planted tumors, and the metastases were partly dependent on the morphologic pattern. Subsequent transplants of both well and poorly differentiated tumors appeared earlier in generations 2 through 8. Pulmonary metastases were present in 26% of animals bearing successful transplants (10% of these were well differentiated, 90% were poorly differentiated). Curiously, well-differentiated hepatomas, 7 mm or greater in diameter, from rats given carcinogen for 4 mo. were more successfully transplanted isologously than those from rats given carcinogen in the diet for 3 mo. As might be expected, autologous transplants of well-developed hepatomas appeared earlier and grew more rapidly than the corresponding isologous transplants. All homologous s.c. transplants in Sprague-Dawley rats and heterologous intracerebral transplants in Hauschka mice failed to grow within 8-12 mo. (Author summary)

63-1535 THE POTENCY OF 20-METHYLCHOLANTHRENE RELATIVE TO OTHER CARCINOGENS ON BLADDER IMPLANTATION. (E.) Bonser, G. M. (Dept. Exp. Path., U. Leeds, England), D. B. Clayson and J. W. Jull. Brit. J. Cancer 17(2):235-241, 1963.

After surgical implantation into the bladder of the mouse of paraffin wax pellets containing suspected carcinogens such as aromatic amines and their metabolites, the yield of malignant tumors was low, not exceeding 32%, when the experiments were terminated at 40 wk. The method was therefore further investigated by using 20-methylcholanthrene (20-Me) as a "strong" carcinogen and the yield of malignant tumors was raised to 54%. Nonneoplastic changes were of a similar order whether weak or strong carcinogens were used, except for an unusually high incidence of squamous metaplasia when 1-amino-2-naphthol was the carcinogen. Papillomas and invasive carcinomas were more abundant when 20-Me was the carcinogen. Of 37 invasive carcinomas of the latter series, 16 had invaded another organ, such as peritoneal adipose tissue, vagina, uterus, breast, etc. The size of invasive 20-Me tumors was greater and the latent period was less. These results show that the method is a satisfactory one for detecting and assessing the carcinogenic activity of suspected carcinogens. (See also CRA 1(5):#826, 1963.) (Author summary)

See also abstract nos.: 1434, 1451, 1551

VIRAL CARCINOGENESIS

- 63-1536 DELAYED TRANSFORMATION BY POLYOMA VIRUS. (E.) Stoker, M. (Inst. Virol., U. Glasgow, Scotland). Virology (New York) 20(2):366-371, 1963.

When single BHK21 cells exposed to polyoma virus were isolated in microdrops they gave rise to normal, transformed and mixed clones. Mixed clones constituted more than 33% of the total clones with transformed cells, and when recloned they gave rise to pure cultures of normal and transformed cells. When mixed clones were propagated without recloning, the transformed cells rapidly replaced the normal cells. Mixed clones are probably due to delayed transformation occurring up to 7 or 8 generations after exposure of the cell to virus. This late transformation may be due to persistence of intact virus or some part of it in the dividing cells. (See also CRA 1(1):#116, 1963.) (Author summary)

- 63-1537 RESISTANCE OF MICE INFECTED WITH MOLONEY LEUKEMIA VIRUS TO FRIEND VIRUS INFECTION. (E.) Rowe, W. P. (Natl. Inst. Allergy Infect. Dis., Bethesda, Md.). Science 141:40-41, 1963.

Mice inoc. with the Moloney strain of mouse lymphoid leukemia virus showed marked diminution of spleen wt. response to infection with Friend leukemia virus given 3 to 4 wk. later. (Author summary)

- 63-1538 MORPHOLOGY OF THE ONCOGENIC RESPONSE OF HAMSTERS TO POLYOMA VIRUS INFECTION. (E.) Stanton, M. F. (NCI, Bethesda) and H. Otsuka. J. Nat. Cancer Inst. 31(2):365-409, 1963.

The distribution, morphology, and pathogenesis of tumors occurring in 274 hamsters s.c. inoc. with different dilutions of fluid from cultures of mouse embryo cells infected with polyoma virus are described. The histology and apparent behavior of the tumors in animals that survived infection indicated a few had all the qualities of highly malignant fibrosarcomas, while others lost even the simple ability to continue proliferation. Most tumors continued to grow, but formed ever-expanding, circumscribed nodules with limited ability to invade or destroy tissues. These nodules may be exceptionally valuable research tools, since their cells seemed to deviate from normal immature cells only in the ability to continue growth.

- 63-1539 STRUCTURE AND COMPOSITION OF K VIRUS, AND ITS RELATION TO THE "PAPOVAVIRUS" GROUP. (E.) Mattern, C. F. T. (Natl. Inst. Med. Res., Mill Hill, London), A. C. Allison and W. P. Rowe. Virology 20(3):413-419, 1963.

Negatively stained, purified preparations of K

virus, SV40, and polyoma virus were examined in the electron microscope. All three viruses appear to be constructed of more than 42 morphological subunits, probably 92, but possibly 72. Chemical examinations indicate that K virus contains double stranded DNA, 7% by wt. Other similarities between K virus and the oncogenic "papova" viruses are discussed. (Author summary)

- 63-1540 CHROMOSOMAL DISTURBANCES OBSERVED IN HUMAN FETAL RENAL CELLS TRANSFORMED IN VITRO BY SIMIAN VIRUS 40 AND CARRIED IN CULTURE. (E.) Yerganian, G. (Harvard Sch. Med., Boston), H. M. Shein and J. F. Enders. Cytogenetics (Basel) 1(6):314-324, 1962.

Karyological disturbances were observed during 6th and 17th subcultures in 3 lines of SV40-transformed human fetal renal cells which were not evident in the 1st to 3rd subcultures of uninoculated control cells. The available evidence supports the hypothesis that the observed aberrations reflect changes in the cell genome attributable to cell virus interaction at the time of transformation. While it seems unlikely that environmental conditions alone were responsible for the chromosomal aberrations, that they may have played a role in selecting certain kinds of abnormalities is suggested by the increasingly higher frequency of monosomy for one member of Nos. 21 in the lines subjected to the longest cultural experience.

- 63-1541 INHIBITORY EFFECT OF AMINOPTERIN AND 5-BROMODEOXYURIDINE ON THE MULTIPLICATION OF SIMIAN VIRUS 40. (E.) Diderholm, H. (Inst. Virol., U. Uppsala, Sweden). Acta Path. Microbiol. Scand. 59(1):87-90, 1963.

In monkey kidney cell cultures multiplication of simian virus 40 (SV40) was inhibited by aminopterin and, more effectively, by 5-bromodeoxyuridine. Virus titers in the supernatants and intracellularly, and also cytopathic virus changes were inhibited, although cell culture counts were not affected. Results indicate that the nucleic acid of SV40 is DNA. (See also CRA 1(5):#923, 1963.)

- 63-1542 CONCERNING THE SO-CALLED HUMAN "MUSCLE MYXOMA AND MYXOSARCOMA WITH CELLULAR INCLUSIONS. (Ger.) Glazunov, M. F. (Path. Morph. Lab. Inst. Oncol., Acad. Med. Sci. USSR, Leningrad) and J. G. Pučkov. Zschr. Krebsforsch 65(5):439-445, 1963.

In six cases of myxomas of human "muscle" special features were detected enabling one to group the neoplasms with those tumors produced in animals and birds by viruses (Shope fibroma, myxomatosis Sanarelli, and filterable chicken sarcoma). The special features noted were: 1. The multicentric

origin of the tumors. 2. The zonal structure of a tumor, in which it changed in a layer-like manner from the periphery to its center. 3. The peripheral, autochthonous, appositional growth, in which the tumor incorporated the edematous, inflamed tissues about it. 4. The spontaneous necrobiosis or softening, with subsequent encapsulation of the tumor. 5. The presence of eosinophilic inclusions (containing no DNA) in the nuclei and cytoplasm of fibroblasts, and in the nuclei of histiocytes. (Author summary)

1543 EXPERIMENTAL STUDIES ON HISTOGENESIS OF ROUS SARCOMA. (Jap.) Higashi, H. (Dept. Path., Sapporo Med. Coll., Japan). Sapporo Med. J. (Sapporo Med. J.) 23(1):20-41, 1963.

On Rous No. 1 chicken sarcoma virus was injected into chickens, first histological evidence of tumor formation was seen 4-5 days later, which was followed by a rapid growth during the successive days. The growth of the tumor was found to take place at a gradual pace after the appearance of serum antibodies, suggesting that the tumor growth in this stage might be attributed to the multiplication of the tumor cells themselves but not to the repeated infection of normal cells with the virus. Inflammatory cells were found to be permanent constituents of the tumor and were especially marked when serum antibodies appeared. The inflammatory reaction in this particular stage was characterized by hyaline degeneration of connective tissues and around vessel walls and formation of fibrin thrombi, presumably resulting from an allergic reaction. From a cytological and electron-microscopical point of view, it was noted that the infection with the virus stimulated the fibrocytes bringing about simple hypertrophy and hyperplasia at the initial stage of the tumor growth, without any special characteristics as tumor cells. The essential changes may occur in the cells and as the transformation of the hypertrophic cells to the ultimate tumor cells might be attained. Metastasis of the tumor, which was seen in the lung and other internal organs, was assumed to result mainly from viremia, however, the possibility cannot be eliminated that the tumor cells themselves participate to some extent in the formation of the metastasis.

1544 EXPERIMENTAL STUDIES ON SPREAD OF ROUS SARCOMA IN RATS. (E.) Saldeen, T. (Inst. Path., U. Lund, Sweden). Acta Path. Microbiol. Scand. (Suppl. 162):87 pp, 1963.

Studies of the natural mode of spread of Rous virus-induced rat sarcoma from earlier passages revealed that the tumor metastasized to lymph nodes and lungs. Serial transplantation had no effect on the spread of the tumor. In lymph nodes the thoracic duct a few tumor cells were found during the first 2 days after i.p. injection of living tumor cells. Tumor cells injected into a

tail vein gave rise mainly to lung tumors; intraperitoneal injection resulted in liver tumors only. The frequency of lung and liver tumors depended on the size of the inoculum. In rats with established i.p. tumors, treatment with hydrocortisone (HC) resulted in an increase in the number of tumor cells in the thoracic duct lymph. Rats with i.m. tumors in the thigh and treated with HC often had tumor cells in the lymph. HC increased the frequency of pulmonary metastases after i.v. injection, and the frequency of spread to the liver and subcutis after intracardial injection of tumor cells. Hyaluronidase increased the extent of tumor growth in the mediastinal lymph nodes in rats with i.p. tumors. Liver cirrhosis increased the percentage of intrahepatic growths following intraperitoneal injection of tumor cells. After i.v. injection of tumor cells, hepatic metastases appeared in most of the animals with cirrhosis, but in none of those with normal livers. A comparison of these findings with data from the literature on tumors not known to be of viral origin revealed no general difference in respect to spread.

63-1545 IMMUNOLOGICAL STUDIES ON TUMORS BY MEANS OF FLUORESCENT ANTIBODY METHOD. I. LOCALIZATION OF VIRAL ANTIGENS IN C58 MOUSE LEUKEMIA. (Jap.) Kotsuka, T. (Hiraki Clin., Dept. Intern. Med., Okayama U. Sch. Med., Japan), Z. Ota, M. Kahara, Y. Takahashi and T. Makihata. Gan No Rinsho (Jap. J. Cancer Clin.) 9(6):302-307, 1963.

Viral antigens in C58 mouse leukemia including spontaneous lymphatic leukemia, OHS-LL No. 1 (lymphatic) leukemia and OHS-LL No. 2 (myeloid) leukemia were detected by means of fluorescent antibody techniques. Leukemia viruses were isolated best by extraction with fluorocarbon. Viral antigens were more readily observed employing the complement fixation method of fluorescent antibody study than by use of the direct or indirect methods. There was evidence of localization of viral antigens both within and outside the leukemic cell; these antigens were found (in decreasing order of concentration) in the bone marrow, lymph node, spleen and liver, but not in the lung, kidney or brain. Viral antigens were detected in greater amounts in spontaneous lymphatic leukemia than in the other two kinds of leukemia. In the latter, there was no apparent difference in distribution of the viral antigens between the lymphatic and myeloid leukemias.

63-1546 THE RELATIONS BETWEEN THE PATHOGENIC AND ANTIGENIC EFFECTS OF THE VIRUS OF MYELOID LEUKEMIA IN MICE. (Ger.) Bielka, H. (Inst. Exp. Cancer Res., German Acad. Sci. Berlin, Berlin-Buch), Chang Yü Yen and F. Hoffmann. Acta Biol. Med. German. 10(5-6):584-589, 1963.

The influence of physical, chemical and enzymatic treatment upon the pathogenic and antigenic effect of the virus of myeloid leukemia was determined in

mice. Both effects are inactivated by heating, trypsin, ether, deoxycholic acid and saponin. Formalin only leads to an inactivation of the pathogenic effect, whereas the antigenic effect is not influenced. Hence the pathogenic and antigenic qualities of the virus would appear to be different in respect to their chemical structure. Nucleic acid is described as the pathogenic virus component, the lipoproteid as the antigenic virus component. (See also CRA 1(3):#487, 1963.) (Author summary)

- 63-1547 INDUCTION OF TUMOURS IN SYRIAN HAMSTERS BY TWO VARIANTS OF ROUS SARCOMA VIRUS. (E.) Klement, V. (Inst. Exp. Biol. Genet., Czech. Acad. Sci., Prague) and J. Svoboda. *Folia Biol. (Praha)* 9(3):181-188, 1963.

The authors' strain of Rous sarcoma (RS) induces fibrosarcomas or polymorphocellular sarcomas in Syrian hamsters within one mo. after admin. The incidence of sarcomas in hamsters decreases with the age at which the RS was admin., from 30% when inj. within 24 hr. after birth, to zero in fully grown animals. Sublethal irradiation of adult animals did not influence their resistance to the authors' strain of Rous virus. The tumors were difficult to passage, a few passages only being achieved both in young and adult animals. The tumors grew invasively, killing the host, and metastasized into the lungs. The Schmidt-Ruppin strain of RS induces sarcomas in 100% of Syrian hamsters at all ages. Tumors induced by this strain of virus grow more rapidly and metastases are more frequent. The admin. of a purified virus preparation and filtrate of the authors' strain of Rous virus did not induce tumors in hamsters.

- 63-1548 AN ANALYSIS OF SV40-INDUCED TRANSFORMATION OF HAMSTER KIDNEY TISSUE IN VITRO. I. GENERAL CHARACTERISTICS. (E.) Black, P. H. (Natl. Inst. Allergy Infect. Dis., Bethesda, Md.) and W. P. Rowe. *Proc. Nat. Acad. Sci. USA* 50(4):606-613, 1963.

When hamster kidney monolayers are exposed to the simian vacuolating virus--SV40, abnormal proliferation of tissue occurs after a variable latent period. The length of the latent period is dependent on the type of medium, virus strain, and dosage of virus used. The transformed cells produce mixed tumors (carcinosarcomas) when transplanted to hamsters. SV40 proliferated continually in the primary cultures and became progressively more difficult to detect in transformed cultures; in late passages of transformed cells, virus could only be recovered when these were planted directly on *Cercopithecus* kidney monolayers. (Author summary)

- 63-1549 AN ANALYSIS OF THE ACTION OF ROUS SARCOMA VIRUS IN VIVO. (E.) Harris, R. J. C.

(Imp. Cancer Res. Fund, Mill Hill, London) and F. C. Chesterman. *Proc. Roy. Soc. Med.* 56(4):307-308, 1963.

A review is presented of a number of studies which led to the isolation of extracts from chick b cells which contained an antigen which rendered turkey embryos or newly hatched turkeys tolerant to later challenge with cell-free Rous sarcoma virus (RSV). Work from other laboratories is reviewed which indicates that this antigen was not present in all strains of RSV. RSV strain AL from Sweden produces multiple cysts and tumors in hybrid rats inoc. when newborn. This rat tumor was readily transplantable into newborn rats, less so into hamsters and first grew but then regressed in chicks. These tumors are composed of rat, not of chicken cells, as indicated by the absence of the micro-chromosomes which are numerous in chicken tumor cells.

- 63-1550 ISOLATION OF THE VACUOLATING VIRUS (SV40) FROM DIFFERENT MATERIALS. (E.) Deichman, G. I. (Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). *Acta Virol. (Praha) [Eng.]* 7(3):250-253, 1963.

Additional studies are reported on the isolation of SV40 from different materials (see CRA 1(5):#964, 1963). Urine from 2/12 tumor-bearing hamsters yielded virus; in one of these cases virus was isolated from the tumor extract. Virus could not be isolated from cultures of kidney from 3-5-day-old hamsters inoc. with SV40 on 1 of 1 of life. No virus was recovered from 2 hamster embryo cultures inoc. with SV40.

- 63-1551 INFLUENCE OF URETHANE ON SUSCEPTIBILITY TO LEUKAEMIA INDUCTION BY GRAFFI VIRUS IN ADULT MICE. (E.) Chieco-Bianchi, L. (Inst. Pathol. Anat., U. Bari, Italy), L. Fiore-Donati, G. De Benedictis and G. Tridente. *Nature (London)* 199:292-293, 1963.

When groups of male and female mice were given urethan (U; 1 mg/g x 4 at intervals of 3-4 days, i.p.) followed 24 hr. after the last inj. with 0.1 ml of a cell-free extract which contained Graffi virus, leukemia incidence during 10 mo. period of observation in C57BL and C3H mice, was, resp., 16% of 19 and 7% of 28. When the sequence was reversed, with an interval of 4 days between inoc. of the extract and the first dose of U, incidence was 55.5% of 18 and 0/20, resp. With U alone, results were 8% of 24 and 5% of 20, resp.; after virus alone, 5% of 38 and 0/27, resp. The mean latent period in all groups was about 7 mo. The marked increase in incidence of leukemia in C57BL mice only when U was admin. after the virus confirms, under different experimental conditions, a previously described "promoting" action of this chemical.

63-1552 BIOLOGICAL STUDIES ON HeLa CELLS. (E.) Nakano, A. (Dept. Path., Okayama U. Sch. Med., Japan). Bull. Cancer Inst. Okayama 11(1):70-85, 1961.

A homogenate of cultured HeLa cells was inj. into the brain of guinea pigs. The brain of animals which survived 7-10 days was homogenized and a cell-free supernatant was prepared which was inoc. serially into the brain of other guinea pigs. Some inj. animals developed pneumonia which was distinguishable from that due to virus contamination. Some animals of the 2nd and 3rd generation showed leukemoid reaction. Antiserum prepared from rabbits had a cytopathic effect on HeLa cell cultures.

63-1553 EVIDENCE FOR A RING STRUCTURE OF POLYOMA VIRUS DNA. (E.) Dulbecco, R. (Salk Inst. Biol. Stud., La Jolla, Cal.) and J. Vogt. Proc. Nat. Acad. Sci. USA 50(2): 236-243, 1963.

Polyoma virus DNA always sediments in two bands, fast (F) and slow (S); both are stable under a variety of conditions and both are infectious. In the column of methylated albumin S is eluted at higher salt conc. than F. In density gradient equilibrium centrifugation studies, at pH 7.5 the F and S bands had the same density and did not differ greatly in width; at pH 11.8 most had the density of native DNA, whereas S had the density of denatured DNA. At pH 12.5 both F and S were denatured; S formed the wider band. The infectivity of the F component is increased several times after treatment at pH 12.5 followed by neutralization; the infectivity of S is lost after this treatment. Pancreatic DNase converts F into S with loss of infectivity. The kinetics of conversion is unusual, since it is of the first order. These results show that molecules of polyoma virus DNA in different states exist in the F and S component. The data are consistent with the hypothesis that the F component is made up of molecules in ring form, and the S component of molecules in linear, or open, form.

63-1554 THE CYCLIC HELIX AND CYCLIC COIL FORMS OF POLYOMA VIRAL DNA. (E.) Weil, R. (Gates and Crellin Lab. Chem., California Inst. Technol., Pasadena) and J. Vinograd. Proc. Nat. Acad. Sci. USA 50(4):730-738, 1963.

Results obtained from various sedimentation analyses and related studies show that polyoma viral DNA contains linear and cyclic helical molecules. The double-stranded cyclic helix denatures in alkaline solutions to form a double-stranded cyclic coil, a new type of coiled molecule in which all of the turns originally present in the helix are conserved.

63-1555 POLYOMA VIRUS. I. CELL--VIRUS INTERACTION AT LOW TEMPERATURE. (E.) Helgeland, K. (Virus Dept., Natl. Inst. Public Health, Oslo, Norway), O. LaHelle and J. Jonsen. Acta Path. Microbiol. Scand. 58(4):511-516, 1963.

When hemagglutinin titrations (HA; both extra- and intracellular) were made on infected mouse embryo cells which had been incubated for 1-10 days, a constantly lower titer was obtained when the initial 30-min. interaction with SE polyoma virus took place at 37°C compared with interaction at 4° and 22°C. When the interaction time at 4°C was varied between 1 and 300 min., max. virus HA occurred after 20 min. When interaction time at 22°C was varied between 1 and 180 min., max. virus HA occurred after 40 min.

63-1556 THE RESPIRATION AND AEROBIC GLYCOLYSIS OF MOUSE EMBRYO CELL CULTURES INFECTED WITH THE SE POLYOMA VIRUS. (E.) Skarzynski, B. (Dept. Physiol. Chem., Med. Acad., Krakow, Poland), M. Guminska and Z. Porwit-Bohr. Acta Chem. Scand. 17(Suppl. 1):55-58, 1963.

See CRA 1(3):#510, 1963.

63-1557 MYELOID CHLOROLEUKEMIA VIRUS IN TRANSPLANTABLE MICE TUMOURS. (E.) Prigogina, E. (Inst. Exp. Clin. Oncol., Moscow). Acta Un. Int. Cancr. 19(1-2):397-400, 1963.

Strains C57, CC57, C3Hf and C3HA mice were sensitive up to 2.5 mo. of age to inoc. with leukemogenic virus of the Graffi-myeloid-chloroleukemic type which was found as a contaminant in various tumor strains. Leukemia appeared in 56.5% of 115 mice used in 5 passages. Virus inoc. into newborn mice induced leukemia in 60-90% after 3-8 mo.; inoc. into 3-10 wk. old mice, 30% after 2-3 mo. Chloroleukemias were seen in 20-25%; approx. 50% were myeloid; reticulosis was seen in more than 25%; the remainder were hemocytoblastic. Transplantation of tumor tissue was strain specific. The incidence of leukemia among mice inoc. with cell-free material of Ehrlich carcinoma was 16/28; Puiman leukemia, 10/14; mammary cancer RSM, 8/23; and forestomach carcinoma Og-5, 1/11. Extracts of organs of normal C57BL and C3Hf mice did not induce leukemia in 33 mice but the latter extract induced polyoma tumors in 2/16. Tumors RMG, MAP, S-298 and PRG were non-leukemogenic but the last 2 induced polyoma tumors in 1/5 and 3/15, resp. Attempts to isolate myeloid chloroleukemia virus were unsuccessful. Cultures of leukemic cells released virus through the first 17 generations but none was detected in the 48th generation.

63-1558 GENETIC RESISTANCE TO ROUS SARCOMA VIRUS IN EMBRYO CELL CULTURES AND EMBRYOS.

(E.) Crittenden, L. B. (ARS, Reg. Poultry Res. Lab., East Lansing, Mich.), W. Okazaki and R. Reamer. *Virology* 20(3):541-544, 1963.

When Rous sarcoma virus (RSV) was assayed on the chorioallantoic membranes (CAM) of White Leghorn lines 6 and 7, a dilution close to 10^{-1} was needed to induce in line 7 embryos a response (median 1.5 pocks) that was comparable to that induced in line 6 with a 10^{-5} dilution (median 2.5). Following the procedure of Waters, 2 single-male matings of lines 6 and 7 were made; then line 6 and 7 males were interchanged. When pock counts were made of the CAM's of all crosses, the line 7 embryos showed a lower median count than the other 3 classes of embryos even though they were inoc. with 2000x the virus dose. Median pock count of the crosses male of line 6 x dams of lines 6 and 7 was, resp., 51 and 76. With the sire line 7 x dams 6 and 7, counts were 84 and 20. Tissue cultures of the various embryos showed a parallel susceptibility to the same RSV preparation. These data suggest that genetic variability in susceptibility to RSV occurs among chicken embryo cell cultures as well as among embryos and hatched chickens, and that the genetic variability in response to inoc. by these 3 methods is correlated.

63-1559 CHANGES IN RESISTANCE TO THE PROLIFERATION OF ISOTRANSPLANTED GROSS VIRUS-INDUCED LYMPHOMA CELLS, AS MEASURED WITH A SPLEEN COLONY ASSAY. (E.) Axelrad, A. A. (Div. Biol. Res., Ontario Cancer Inst., Canada). *Nature (London)* 199:80-83, 1963.

Eleven adult C3H mice, which had not succumbed after 4.5 mo. to the i.p. inj. of 10^3 viable C3H lymphoma cells (from mice inj. as infants with Gross passage A virus), were re-injected with 10^5 cells from another lymphoma, and again 3 mo. later with 10^4 cells from another lymphoma. Six days after the last inj. the mice were challenged i.v. with 5×10^6 viable cells from still another lymphoma. When the spleens were examined 12 days later, the pretreatment with sublethal doses of viable lymphoma cells from isologous donors caused a 7-fold reduction in the number of colonies formed compared to untreated controls which received the same challenge. Pretreatment with a single i.p. dose of a Gross virus extract 6 days before challenge also caused a reduction in the number of colonies formed in the spleen. When the Gross virus extracts were given to newborn mice which were challenged with isologous lymphoma cells later in life, they responded by causing an increase in the fraction of those cells that are capable of proliferating in them.

63-1560 RAPID TRANSFORMATION OF HUMAN FIBROBLAST CULTURES BY SIMIAN VIRUS 40. (E.) Jensen, F. (Wistar Inst., Philadelphia), H. Koprowski and J. A. Pontén. *Proc. Nat.*

Acad. Sci. USA 50(2):343-348, 1963.

When various strains of human fibroblasts cell cultures were infected with SV40 when the cultures were "aged" (approaching the max. number of passages seen in non-infected cultures), the time interval between exposure and transformation was shortened. Thus in substrain XXVI of strain WI-26, cultures infected at passage 55 (max. 56), transformation occurred in 3-5 wk. When substrain XII was infected at passage 27 (max. 41), transformation interval was 10 wk. Similar shortening of the interval between infection and transformation was seen in substrain IV and parent of WI-38 and substrains D 90 and D 285 of strain W-5 CM.

63-1561 ATTEMPTS TO TREAT CHARLOTTE FRIEND LEUKEMIA BY THE IMPLANTATION OF HEMATOPOIETIC CELLS FROM ISOGENIC DONORS VACCINATED AGAINST THE VIRUS. (Fr.) Mathé, G. (Cancer Res. Ctr., Claude-Bernard Assn., Saint-Louis Hosp., Paris), J.-L. Amiel and C. Friend. *Bull. Ass. Franc. Cancer* 49(4):416-420, 1962.

Bone marrow cells (2.7×10^7) obtained from isologous strains vaccinated with Charlotte Friend leukemia virus were inj. into Swiss and DBA/2 strain mice following inoc. of live virus and total body X-irradiation (700 r). In the case of the Swiss mice this treatment reduced the number of leukemias which developed (47.5%) when compared with unirradiated and untreated control (60%) or irradiated but treated with bone marrow from normal animals (76.9%). In the case of the DBA/2 animals there was not a significant difference in terms of leukemia incidence, but there was significant difference in the survival times found, the highest increase being observed in mice receiving bone marrow from vaccinated animals.

63-1562 GROWTH PROPERTIES OF POLYOMA VIRUS-INDUCED HAMSTER TUMOR CELLS. (E.) Todaro, G. J. (Dept. Path., New York U. Sch. Med. N.Y.), K. Nilausen and H. Green. *Cancer Res.* 23(6):825-832, 1963.

Hamster polyoma virus-induced sarcomas, when serially cultivated under rigidly controlled conditions, uniformly gave rise to established lines within 10-20 generations of life *in vitro*. Normal hamster embryo fibroblasts, carried in culture under identical conditions, initially grew as well as the tumor cells but always failed to develop into established lines; none continued to grow past 10 generations *in vitro*. The neoplastic cells appeared to be more mutable than the normal fibroblasts and developed into established lines by undergoing changes leading to greater ability to grow autonomously *in vitro*. In the course of establishment of such lines, the cells underwent a reduction in the rate at which they produced tumors when inj. into animals. However, this capacity could be fully

restored by a single animal passage while the cells retained the properties previously acquired in vitro. Embryonic fibroblasts when injected in vitro with polyoma virus also develop into established lines. Such lines, tested in the newborn hamster, were found to have neoplastic properties comparable to those of tumors produced in vivo. One cell line, after transformation by the virus, was initially unable to produce tumors but on continued growth in vitro acquired increasing capacity to do so. Full neoplastic potential was not reached until the transformed cells had grown through over 40 cell generations in vitro. The capacity of polyoma cells to produce tumors was not repressed when these cells were inj. in mixtures with normal cells in great excess. (Author summary)

3-1563 ANTIGENIC DIFFERENCES BETWEEN NORMAL AND POLYOMA VIRUS-TRANSFORMED HAMSTER CELLS. I. A QUANTITATIVE STUDY OF THE CYTOTOXIC EFFECT OF ANTISERA. (E.) Bases, R. (California Inst. Tech., Div. Biol., Pasadena). Cancer Res. 23(6):811-817, 1963.

Rabbit antisera against hamster embryo cells and hamster cells which had been transformed by polyoma virus were assayed by single cell techniques. Antiserum killed cells in the presence or absence of complement, and the two mechanisms of inactivation appear to be different. Kinetics of cell-killing by antibody and complement are described. The transformed cells studied appear to have less surface antigen than embryo cells. Specific antibody to polyoma virus-transformed hamster embryo cells could not be found in an antiserum prepared against one such polyoma-transformed hamster cell line. The methodology reported has proved capable of resolving antigenic differences between mammalian cells in the sense that an unabsorbed antiserum having equally strong sensitizing effects on two different cell types could be shown to specifically sensitize only one cell type after exhaustive absorption with the other. (Author summary)

3-1564 SPONTANEOUS KIDNEY TUMORS IN THE FROG: RATE OF OCCURRENCE IN ISOLATED ADULTS. (E.) Rafferty, K. A., Jr. (Dept. Anat., Johns Hopkins U. Sch. Med., Baltimore). Science 141:720-721, 1963.

Kidney tumors in the frog are thought to be virus-caused and naturally transmitted. The present report indicates that natural transmission between mature adults is not a factor in spontaneous tumor development and implies primary infection at earlier stages if a virus is indeed involved. Parasitism and nutritional state appear to be of little significance. See also CRA 1(5):#928, 1963. (Author summary)

3-1565 TRANSPLANTABLE STRAIN OF SHOPE'S RABBIT CARCINOMA. (E.) Nadareishvili, A. E.

(Inst. Exp. Path., Acad. Med. Sci. USSR, Moscow). Biull. Eksp. Biol. Med. 53(5):595-598, 1963.

Transplantation of skin cancer into the muscles of the thigh of newborn rabbits led to tumor development. Further transplantations have made it possible to obtain a transplantable strain of Shope's cancer. By now 31 generations have already been transplanted. The tumors attained a considerable size (7 x 8 cm); they were tuberous and adhered closely to the surrounding tissue. A typical picture of squamous cell cornifying carcinoma was observed histologically. There were no metastases. Papillomas were induced in a number of cases by inoc. of the skin with an extract of these tumors. (Author summary)

63-1566 VIRAL INFECTIONS IN THYMECTOMIZED ANIMALS. (E.) Denys, P., Jr. (Virus Dept., Rega Inst., U. Louvain, Belgium), R. Leyten, M. Vandeputte and P. De Somer. J. Gen. Microbiol. 32(1):ii-iii, 1963.

In a group of 28 rats, thymectomized at birth and inoc. s.c. 2-3 wk. afterwards with 10⁸ TCID₅₀ of polyoma virus, 7 up to now have developed a polyoma tumor, while none have occurred in sham-operated controls. All the tumors found were large cerebral hemangiomas; this tumor type and localization are only rarely encountered in the strain of Wistar rats used when inoc. at birth. Positive hemagglutination titers were found in 5/7.

63-1567 POLYOMA VIRUS. (Ger.) Schmidt, F. (Exp. Oncol. Res. Ctr., German Acad. Sci., Berlin). Zschr. Ges. Inn. Med. 18(13):586-597, 1963.

From the author's own findings and those in the literature, it is concluded that there is an interference between polyoma virus and species of leukemia virus. From this is derived a working hypothesis concerning the genetic relationships between these virus species discussed in the light of current research. This working hypothesis--the origin of mouse-leukemia-virus-species from messenger RNA of the polyoma virus--would permit a free classification within the bounds of induction theories of carcinogenesis; its currently speculative character is emphasized. A review is given of polyoma virus (172 references). (Author summary)

63-1568 SIMILARITY OF DNAs ISOLATED FROM TUMOR-INDUCING VIRUSES OF HUMAN AND ANIMAL ORIGIN. (E.) Green, M. (Dept. Microbiol., St. Louis U. Med. Sch., Missouri) and M. Piña. Proc. Nat. Acad. Sci. USA 50(1):44-46, 1963.

The DNAs of nontumorigenic types 2 and 4 adenoviruses contained 56-57% guanine-cytosine, while those of tumorigenic types 12 and 18 adenoviruses were surprisingly different and contained 48-49%

guanine-cytosine. A striking similarity between the DNAs of the tumor-inducing viruses of human origin, i.e., adenovirus types 12 and 18, and those of animal origin, polyoma virus and Shope papilloma virus, is noted: all 4 tumor viruses have very similar buoyant densities, denaturation temperatures, and base compositions. (See also CRA 1(4):#720 and *ibid.* #730, 1963.)

- 63-1569 VIRAL SUSCEPTIBILITY AND EMBRYONIC DIFFERENTIATION. 1. THE HISTOPATHOLOGY OF MOUSE KIDNEY RUDIMENTS INFECTED WITH POLYOMA AND VESICULAR STOMATITIS VIRUSES IN VITRO. (E.) Saseň, L., T. Vainio and S. Toivonen. *Acta Path. Microbiol. Scand.* 58(2):191-203, 1963.

A study is presented of the histological changes seen in mouse kidney rudiment in vitro after infection with SE-polyoma virus and vesicular stomatitis virus (VSV). The microscopical lesions are described at the different intervals of the in vitro cultivation of infected rudiments. Both stage-dependent and agent-specific features were noted in the viral susceptibility of the different tissue components. The rather slow polyoma infection started from the undifferentiated stromal mesenchyme, and both the condensed, pretubular areas and the differentiated secretory tubules seemed to resist the infection. VSV first affected the condensed areas of metanephrogenic mesenchyme, and subsequently spread throughout the kidney rudiment. The observations are discussed in the light of viral teratology and earlier observations in vivo. No correlation of the present observations to the events of normal morphogenesis can be effected until the normogenesis is more thoroughly analyzed.

- 63-1570 DEMONSTRATION OF THE ABSENCE OF INFECTIOUS ROUS VIRUS IN RAT TUMOR XC, WHOSE STRUCTURALLY INTACT CELLS PRODUCE ROUS SARCOMA WHEN TRANSFERRED TO CHICKS. (E.) Svoboda, J. (Inst. Exp. Biol. Genet., Czech. Acad. Sci., Prague), P. Chýle, D. Šimkovič and I. Hilgert. *Folia Biol. (Praha)* 9(2):77-81, 1963.

For an earlier study on the relationships between virus and cell in rat sarcomas induced by Rous virus, see CRA 1(5):#912, 1963. Infectious Rous virus (RV) was not found in cell-free preparations prepared from rat sarcoma XC, including filtrates, all the main cell fractions and conc. microsomal fraction, although an adequate dose of intact cells induces Rous sarcoma in chicks. Virus was likewise not found in high speed sediments from 700 ml culture fluid from a line of XC cells cultivated in vitro over a long period. The serum of rats which rejected tumor XC showed no neutralizing activity in tests with RV. Fowl antisera which neutralized RV when added to tissue cultures of proliferating XC cells did not affect their ability to induce Rous Sarcoma in chicks. No virus with oncogenic activity in rats was found in extracts of tumor XC. No hemaggluti-

nating agent of the type of polyoma virus was found in preparations of Rous sarcoma, of RV used for experiments or in culture fluids from tumor XC and of Rous sarcoma cell cultures.

- 63-1571 ATTEMPTS TO INDUCE FORMATION OF ROUS SARCOMA VIRUS IN CELLS OF TUMOUR XC. (E.) Chýle, P. (Inst. Exp. Biol. Genet., Czech. Acad. Sci., Prague), V. Klement and J. Svoboda. *Folia Biol. (Praha)* 9(2):92-98, 1963.

No infectious Rous virus (RV) production was induced in tumor XC cells cultivated in vitro after X-irradiation with doses of 300-10,000 r and UV irradiation with doses of 6000-96,000 erg/cm². The results of in vivo X-irradiation of tumor XC were also negative. Cultivation of XC cells in various enriched media in the temperature range of 30° to 41.5°C likewise did not lead to the formation of infectious RV. (See also CRA 1(8):#1570, 1963.)

- 63-1572 CLONAL ANALYSIS OF LINE XC_{tc} RAT TUMOUR CELLS (DERIVED FROM TUMOUR XC) GROWTH IN VITRO. (E.) Šimkovič, D. (Inst. Oncol. Czech. Acad. Sci., Prague), J. Svoboda and N. Valentová. *Folia Biol. (Praha)* 9(2):82-91, 1963.

Cells of rat tumor XC capable of forming mature Rous virus after contact with fowl cells were adapted to long-term growth in vitro and three non-cloned lines of cells were obtained (XC_{tc}, XC_{tc}T and XC_{tc}P). All three lines retained their ability to induce typical fowl Rous sarcoma in chicks after cultivation in vitro for many mo. Three subclonal cell populations (S16, S17 and S30 from an initial 16, 17 and 30 cells) and three single-cell clones (K-1, K-2 and K-4) were isolated from cells of the line XC_{tc}T. Tests in chicks showed that all these types of cells derived from the line XC_{tc}T induced tumors in inoc. chicks. In order to induce tumors in 50% of 4-7-day-old chicks, 5 x 10⁵ - 2.5 x 10⁶ XC_{tc}T or S16 cells are required. The incidence of tumors after these doses of cells of lines XC_{tc}P and subclone S17 was lower. When 7-week-old chicks were used as recipients, the incidence of tumors was altogether lower. No tumors were observed in chicks inoc. with 10⁵ cells of lines XC_{tc}, XC_{tc}P and XC_{tc}T and of subclones S16 and S17. In tests in newborn rats, doses of 5 x 10⁵ cells of the parental line XC_{tc}T and of its subclones S16, S17 and S30 induced tumors in practically 100%. Attempts to induce tumors in chicks by means of cell-free medium from cultures of non-cloned cells and cloned lines isolated from XC_{tc}T cells were negative.

- 63-1573 VIROLOGICAL APPROACHES TO TUMOUR STUDIES. (E.) Zhdanov, V. M. (Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR, Moscow), G. A. Piskunova, Z. I. Merekalova and F. I. Leikina.

Un. Int. Cancr. 19(1-2):284-286, 1963.

properties of oncogenic viruses have been investigated. In a search for cellular reactions would allow the detection of viruses, a of mitotic activity revealed decreases in fibroblasts during the first days after infection with Rous virus. The study of conditions governing the reversible transformation of cells into latent virus proved to be difficult because of the interference of some latent viruses, mainly polyoma virus. The attempt to detect virus at different stages of carcinogenesis was successful.

74 NEOPLASMS IN GUINEA PIGS INDUCED BY AN AGENT IN ROUS CHICKEN SARCOMA.

Ahlström, C. G. (Inst. Path., U. Lund, Sweden), S. Bergman and B. Ehrenberg. Acta Microbiol. Scand. 58(2):177-190, 1963.

Guinea pigs were inoc. i.m. with a suspension of finely minced Rous chicken sarcoma (Edwards-Rupp strain) or with presumed cell-free supernatant fluid obtained by repeated centrifugation of suspension of homogenized sarcoma. In about 75% of the guinea pigs tumors developed at the site of inj. within 4-6 weeks. They usually grew progressively. In some cases secondary growths appeared in the lungs. Sometimes the tumors spontaneously regressed. Histologically they usually had the character of spindle cell sarcomas, sometimes of pleomorphic cell sarcomas or pleomorphic sarcomas. Guinea pig sarcoma was successfully transferred to newborn guinea pigs and could be maintained in series through 3 generations. All attempts to transfer the sarcoma from guinea pig to guinea pig by means of cell-free material failed. The guinea pig sarcoma failed. Material from 14-day-old guinea pig sarcoma (1 mo. after inoc. of the virus) inj. into chickens induced a Rous sarcoma at the site of the inj. Attempts to recover the virus from older guinea pig tumors failed. (See also CRA 1(5):#966,

75 ALKALINE PHOSPHATASE IN VIRUS-INDUCED LEUKEMIAS OF MICE. (Ger.) Fey, F.

Exptl. Cancer Res., German Acad. Sci. (Berlin-Buch) and E. J. Schneider. Acta Med. German 11(2):264-273, 1963.

Analyses of cytochemical and biochemical methods in virus-induced leukemias of mice were examined as to their alkaline phosphatase (AP) activity. In spleen, frozen slices of thymus, spleen and lymph nodes, as well as "touch" and smear preparations of liver, bone marrow, of the blood, as well as thymus homogenates of normal and leukemic mice of different strains were tested. Compared to results of normal tissues which showed very poor activity, the following results were obtained with leukemias. The lymphatic

and paramyeloblastic leukemias invariably possess a strong AP activity. As far as the remaining myeloid forms of leukemia are concerned, the occurrence of AP is more heterogeneous; probably, there exists a correlation between the degree of maturation of the leukemia cells and the AP activity. The reticulum cell leukemias manifest the poorest effect; the values obtained largely corresponded to the normal values. With regard to the activities ascertained, there is a good conformity between the cytochemical and the biochemical methods. The occurrence of the AP is fixed to the leukemia cells. Relations between the increased occurrence of AP and the increased content of inorganic phosphate, as well as its influence on the Crabtree-effect in different forms of leukemia are discussed.

63-1576 VIRUS AND HUMAN CANCER. (Ger.)

Schmidt, F. (Res. Inst. Exptl. Oncol., German Acad., Potsdam, Berlin). Krebsarzt 18(5-6):153-169, 1963.

The usually accepted criteria for determining viruses are reexamined in the light of present day research. A survey is also presented of virus-induced benign and malignant tumors (166 references). The role of viruses in human tumors is summarized by a review of the literature and an examination of work from the author's laboratory. The relations between a cancer "inductor" of primarily endogenous origin and exogenous tumor viruses are discussed according to the "induction hypothesis" of cancerogenesis advocated by the author.

63-1577 ISOLATION OF VIRUSES FROM CHILDREN

WITH ACUTE LEUKEMIA. (E.) Murphy, W. H. (Dept. Microbiol., U. Michigan, Ann Arbor) and D. Furtado. U. Mich. Med. Bull. 29(4):201-228, 1963.

Evidence has been presented that suggests that viruses were isolated from pts. with acute leukemia, sarcomas, and lupus erythematosus. The significance of such findings cannot be assessed until more data are obtained to confirm and extend the findings reported. One value of the positive results is that they provide a framework and firm incentive for additional studies of the possible virus etiology of human malignant diseases.

63-1578 NON-RANDOM CHROMOSOMAL ABERRATIONS IN SV40-TRANSFORMED HUMAN CELLS. (E.)

Moorhead, P. S. (Wistar Inst., Philadelphia, Pa.) and E. Saksela. J. Cell. Comp. Physiol. 62(1):57-83, 1963.

A more detailed account of the paper abstracted as CRA 1(5):#965, 1963.

63-1579 STRUCTURE OF THE POLYOMA VIRUS. (E.)

Kiselev, N. A. (Inst. Crystallogr.,

Acad. Sci. USSR, Moscow) and I. S. Irin.
Biochemistry (New York) 27(4):553-558, 1963.

It has been shown that the polyoma virus, SE strain 2510 consists of a nucleus and capsule. The protein capsule is constructed of 42 morphological subunits arranged with a symmetry of 5:3:2 and forming an icosahedron, the external diameter of which is about 430 Å. The morphological subunits in the formed capsule have a size of 50-60 Å and in the radial direction, about 40-50 Å. The form of the morphological subunits, as well as the apertures sometimes observed in them permit the conclusion that these subunits are not structureless spheres. The hypothesis is advanced that the morphological subunits consist of finer hypothetical hypersubunits, possibly being individual protein molecules. (Author summary)

63-1580 STUDIES ON HUMAN LEUKEMIA. I. SPONTANEOUS LYMPHOBLASTOID TRANSFORMATION OF FIBROBLASTIC BONE MARROW CULTURES DERIVED FROM LEUKEMIC AND NONLEUKEMIC CHILDREN. (E.) Beneyesh-Melnick, M. (Dept. Virol. Epidemiol., Baylor U. Coll. Med., Houston, Texas), D. J. Fernbach and R. T. Lewis. J. Nat. Cancer Inst. 31(6):1311-1331, 1963.

Bone marrow cells from 33 leukemic and 68 non-leukemic children were propagated in long-term tissue culture. Fibroblastic monolayer cultures were obtained from 24 of 43 (56%) specimens taken from the leukemic children when in relapse, from 52 of 79 (66%) specimens taken from the leukemic children when in remission, and from 47 of 71 (66%) specimens from nonleukemic children. Of the 123 fibroblastic cultures obtained, 110 were carried in serial passages and observed for 100 to 300 days. Four fibroblastic cultures, 2 derived from 2 children with acute leukemia in remission, a culture from a child with infectious mononucleosis, and a culture from a child with hemolytic anemia and thrombocytopenia, showed a spontaneous lymphoblastoid transformation. This usually occurred in secondary (P₁) cultures. The spontaneously transformed cultures consisted of a mixture of fibroblastic and lymphoblastoid cells of various sizes. The latter cells actively multiplied, either free in the supernatant fluid or on the fibroblastic monolayer, forming three-dimensional clusters. Cytologically, the lymphoblastoid cells strongly resembled the immature cells seen in direct smear preparations from bone marrow aspirates of leukemic children during the acute stage of the disease. All transformed cultures were serially propagated for prolonged periods, and they maintained their altered ap-

pearance. The phenomenon of "emperipolesis" was observed in all transformed cultures. With the depletion of fibroblastic cells, usually between the 10th and 15th serial transfers, the lymphoblastoid cells ceased multiplying and the culture degenerated. (Author summary)

63-1581 RESISTANCE LEVELS OF POLYOMA TUMORS AND TUMORS OF OTHER ORIGIN TO THE CYTOPATHOGENIC EFFECT OF POLYOMA VIRUS. (E.) Hellström, I. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm). J. Nat. Cancer Inst. 31(6):1511-1523, 1963.

Explants of 10 serially transplanted polyoma tumor lines and of 9 tumor lines of other origin were challenged with a broad spectrum of polyoma virus doses, which included the minimum doses still giving cytopathic changes in normal mouse embryonic cells. The appearance of cytopathic changes was followed after infection, and TCID₅₀ values were determined for the different material tested. Most polyoma and nonpolyoma tumors were more resistant than embryonic cells to polyoma infection, and there were no systematic differences in virus sensitivity between polyoma tumors and neoplasms of other origin. The resistance was different degree for different tumors. It also varied among 17 sublines, established from single cells isolated from the same polyoma tumor and propagated in mice. Some of these sublines had the same degree of sensitivity as embryonic cells. The degree of polyoma resistance of these sublines did not appear to be correlated with the ability for spontaneous polyoma release after explantation, as revealed by the plaque and hemagglutination techniques.

63-1582 CORRELATION BETWEEN THE SENSITIVITY OF POLYOMA-INDUCED MOUSE TUMORS TO POLYOMA AND VACCINIA VIRUS IN VITRO. (E.) Hellström, I. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm) and K. E. Hellström. J. Nat. Cancer Inst. 31(6):1525-1532, 1963.

Explants of 15 polyoma-induced mouse tumor lines of known degree of sensitivity to polyoma challenge were infected with vaccinia virus, and the appearance of cytopathic changes and hemadsorption by the infected cells was scored. A correlation was found between the degree of polyoma and vaccinia sensitivity of the different lines. The findings are interpreted as probably reflecting differences in interferon production or virus adsorption between the tumor lines studied, which will be further investigated. (Author summary)

See also abstract nos.: 1422, 1428, 1463, 1467, 1469, 1610

EPIDEMIOLOGY AND BIOMETRY

583 BRONCHOGENIC CARCINOMA: THE DISTRIBUTION OF THE HISTOLOGICAL TYPES IN THE THREE RACIAL GROUPS OF CAPE TOWN. (E.) Uys, J. (Dept. Path., U. Cape Town Sch. Med., Afr.) and J. I. Perold. S. Afr. Med. J. 62:828-832, 1963.

The distribution of histological tumor types of bronchogenic carcinoma in the European and the colored groups in Cape Town (based on postmortem material and surgical specimens) shows a significant preponderance of squamous celled and small cell carcinoma over adenocarcinoma in both races. This trend conforms with that found in high-incidence countries, and on the basis of the Berg classification may be taken as evidence of a high incidence of bronchogenic carcinoma in these two races also, with the greater incidence in the European group. In comparison with the European group, there are few cases of bronchogenic carcinoma among the Bantu in this series. While a lower incidence in this group may be partly responsible for this finding, it is also to a certain extent due to selective influences, principally the relatively early age of death among Bantu patients admitted to hospitals.

584 STATISTICAL CANCER RESEARCH. THE FINNISH CANCER REGISTER AND ITS FUNCTION. (Fin.) Saxén, E. and M. Hakama. Duodecim 87:385-392, 1963.

The role of a nationwide cancer register in statistical cancer research is outlined, and a description is given of the activities of the Finnish Cancer Register during the 10 yr. of its existence.

585 MULTIPLE POLYPOSIS, EXOSTOSIS, AND SOFT TISSUE TUMORS. (E.) Bochetto, J. (Dept. Surg., Kings County Hosp. Med. Ctr., Brooklyn, N.Y.), J. F. Raycroft and L. W. Innocentes. Surg. Gynec. Obstet. 117(4):494, 1963.

A case of Gardner's syndrome has been presented, along with 2 cases of the disease in offspring of the patient, who each have 2 stigmas of the syndrome. The bony tumors and soft tissue lesions aided the clinical diagnosis of polyposis.

586 GARDNER'S SYNDROME: A CASE REPORT. (E.) Macdonald, I. B. (Dept. Surg., Wellesley Hosp., Toronto, Canada), J. D. T. Macdonald and T. C. Brown. Canad. J. Surg. 6(4):480, 1963.

Attention is drawn to Gardner's syndrome by reporting the case of a man with familial intestinal polyposis in whom carcinoma developed in

the sigmoid colon, and in whom a desmoid tumor grew in the operative scar in the anterior abdominal wall 4 yr. after total proctocolectomy. The multiple cutaneous sebaceous cysts and osteomas of long bones, which have been described in the complete syndrome, were not identified in this instance.

63-1587 HEPATITIS AND NEOPLASIA OF THE CERVICAL EPITHELIUM. (E.) Ferguson, J. H. (Dept. Obstet.-Gynec., U. Miami Sch. Med., Fla.) and D. E. Arias. Am. J. Med. Sci. 246(4):459-461, 1963.

Of 56 women with hepatitis an unselected 36 had a cervical smear made for cancer cells and some patients had appropriate tissue examinations. Twelve (33%) of 36 women who had a smear had a positive result (Papanicolaou Class V, IV or III), meaning that the cellular samples contained cells that were considered conclusive for malignancy, or were strongly suggestive for malignancy, or cells that were suggestive of malignancy. This high incidence in hepatitis patients was without explanation.

63-1588 REGIONAL PECULIARITIES OF CANCER INCIDENCE IN KANAGANDA. (Rus.) Biber, O. I. (Inst. Clin. Exp. Surg., Acad. Sci. Kazakh SSR, Alma-Ata). Vop. Eksp. Klin. Khir. 8:15-18, 1962.

The incidence of cancer in the Kanaganda region increased annually from 408 cases in 1955 to 884 in 1960, or in terms of rate/100,000 of population, from 40 to 88.5. From 4,180 reported cases, 3,673 were among non-Kazakh settlers ("newcomers"). Among natives, cancer of the esophagus was most common (54.1%), followed by cancer of the stomach (18%), uterine cervix (8.4%) and lung (5.4%). Among male Kazakhs incidence of cancer of the esophagus was 54.8%; stomach, 21.8%; lung, 7.8%. In female Kazakhs incidence of cancer of the esophagus was 52.9%; uterine cervix, 21.9%; stomach, 12.2%. Among the males of other nationalities incidence of cancer of the lower lip was 30.9%; stomach, 25.4%; skin, 22.6%; lung, 6.6%; esophagus, 6.5%. Among female "newcomers" uterine cervix incidence was 46.5%; skin, 21.2%; stomach, 12.1%; mammary gland, 8.6%. Cancer rates (per 100,000) for esophagus in natives and "newcomers" was 23 and 3, resp.; cancers of other sites were less frequent in natives than in "newcomers". The author also compares the rate of cancers in Yakuts and Kazakhs with the rate in "newcomers" and concludes that the mode of life and food habits (such as the use of hot, strong tea in relation to cancer of the esophagus) are etiologic factors and are common to both native groups.

63-1589 HEAVY SMOKERS WITH LOW MORTALITY AND THE URBAN FACTOR IN LUNG CANCER MORTALITY.

(E.) Cohen, J. (New York U., New York City) and R. K. Heimann. Industr. Med. Surg. 32(10): 415-425, 1963.

In contrast to the usual cigarette theory of lung cancer, 4 studies of sizeable, well-defined populations show an association of heavier smoking with lower mortality (American Tobacco employees, native white South Africans, native white New Zealanders, and Australians). Furthermore, in studies offered in support of the cigarette causation theory (Doll-Hill, Hammond-Horn, Dorn), regular cigarette users show mortality rates roughly similar to the general populations from which they are drawn. These data indicate that factors other than cigarette use must be involved. In contrast with cigarette usage which shows both positive and negative associations with lung cancer mortality rates, urban residence shows a consistently positive association, not only within study samples but as between large populations. While some investigators have assumed the "urban factor" to be air pollution, the existence of lung cancer mortality gradients for factors other than urban residence and cigarette use suggests the fallacy of using single-variable or even dual-variable statistical analysis as a basis for interpretation as to cause. Factors expressed numerically to date include drinking, marital status, socioeconomic level, and the rural-to-urban residence gradient. Their nature is consistent with the possibility that the "urban factor" is a catchall term for individual characteristics or tendencies related to the urban way of life. Several descriptions of this tendency have been advanced, including "nervous tension," "the syndrome of social stress," "heightened metabolic activity," "the restless personality" and "accelerated rate of living." The last-named has particular relevance to cancer, which has been related by specific site to the biological age of the organism. (Author summary)

63-1590 CARCINOMA OF THE LUNG: THE CHANGING PATTERN OF MORTALITY IN ONTARIO. (E.) Grzybowski, S. (Ontario Dept. Health, Toronto) and R. B. Sutherland. Canad. Med. Assn. J. 89(15):741-744, 1963.

Study of the mortality rates for carcinoma of the lung in men in Ontario between 1931 and 1959 reveals a rise from 3.7 in the early 1930's to 26.7 per 100,000 in the late 1950's. Analysis of age-specific mortality rates in 5-yr. cohorts shows that (1) mortality rates in each cohort rise rapidly after the age of 40, ascending in the later yr. of life almost as a straight line; (2) each succeeding cohort experiences an appreciably higher mortality rate than the preceding one. Mortality rates in individual cohorts in Ontario are compared with those in England; the shape of the cohort curves, and the rate of the increase in mortality from cohort to cohort, are almost identical. However, the picture in Ontario appears to be lagging some 10 yr. behind.

63-1591 THE SIGNIFICANCE OF CHRONIC INTOXICATION FROM CIGARETTE SMOKING IN RELATION TO LUNG CANCER AND HEART DISEASES. (Gr.) Tertizidis, G. (Surg. Clin., U. Heidelberg, Germany), W. Kaulbach and G. Ott. Hellen. Chel. 1(2):107-145, 1963.

Many factors indicate that the smoking of tobacco plays a dominant role in the etiology of lung cancer and chronic nonrheumatic heart disease. An analysis of statistics on the cause of death for West Germany indicates that the double noxa of tobacco smoke tar derivatives and nicotine, results in the placing of bronchial carcinoma and the acquired nonrheumatic heart diseases among the leading causes of death. It is quite probable that the surprising frequency of myocardial damage in male pts. with bronchial carcinoma results mainly from a chronic latent intoxication with these substances.

63-1592 CAUSES OF DEATH. MALIGNANT NEOPLASMS 1950-1952 AND 1958-1960. (E. and Fr.) World Health Organization, Geneva. Epidemiol. Vital Statistics Rep. 16(7-8):470-532, 1963.

Mortality from malignant tumors is reported for the yr. 1950-52 and 1958-60 for 24 countries in various parts of the world. The data are presented according to site of the malignancy in the body, age and sex. This supplements a previous report covering the yr. 1954-60. (See CRA 1(4) #733, 1963.)

63-1593 PRECURSORS OF CORPUS CANCER. IV. ADENOMATOUS HYPERPLASIA AS STAGE 0 CARCINOMA OF THE ENDOMETRIUM. (E.) Gusberg, S. B. (Mt. Sinai Hosp., New York) and A. L. Kaplan. Am. J. Obstet. Gynec. 87(5):662-678, 1963.

A group of pts. with adenomatous hyperplasia have been studied prospectively with subsequent development of endometrial cancer in 8 (12%, of those with any significant follow-up). Matched control pairs failed to show this behavior lending statistical support to the concept of this lesion as Stage 0 cancer of the endometrium. Radiotherapeutic sterilization had been utilized in some of these pts. but the study group is still too small to assay its role in the histogenesis of this malignant transformation as opposed to the basic defect in the tissues and metabolism of these pts. In the control group (free of adenomatous hyperplasia) that received radiotherapeutic castration, no pts. developed cancer of the endometrium in the first 10 yr. and only 1, thereafter, an incidence under 1%. This does not indicate that radiotherapy, alone, is important in this context.

63-1594 RETICULOSARCOMATOSIS IN TWINS. (E.) Zachau-Christiansen, B. (Child. Hosp. Copenhagen, Denmark) and P. A. Rasmussen. Acta Paediat. (Stockholm) 52(5):522-528, 1963.

culosarcomatosis occurred in a set of twins are assumed to have been monozygotic. From age of 10 mo. the pts. showed lack of thrive and infections--especially moniliasis. gradually developed signs of cerebral affection, and died at the age of approx. 13 mo. at interval of 3 wk.

595 PRIMARY CARCINOMA OF THE LIVER IN RELATION TO CIRRHOSIS. (E.) Sagebiel, R. (Dept. Path., Harvard Sch. Med., Cambridge, Mass.), R. B. McFarland and E. B. Taft. Am. J. Pathol. 40(5):516-520, 1963.

100 cases of primary hepatic carcinomas occurring in 23,275 autopsies (an incidence rate of .43%), 89 cases yielded sufficient material for the study of hepatic tissue that was not directly adjacent to tumor. Of these, 26% were cirrhotic, 21% manifested a postnecrotic pattern, and 53% manifested a "posthepatic" pattern. None had the pattern of nutritional cirrhosis, as defined by Gall. The data from this study are consistent with the hypothesis that nutritional disease of the liver in humans is not of prime etiologic importance in the development of hepatic carcinomas.

596 THE COMMONWEALTH OF PENNSYLVANIA. NATALITY AND MORTALITY STATISTICS. JANUARY-JUNE, 1963. (E.) Dept. Health, Bureau of Manag., Div. Data Proc., Harrisburg, Pa. 1963:2-11, 1963.

Number of deaths among residents of the state of Pennsylvania from malignant neoplasms rose from 131.7/100,000 population in 1940 to 176.1 in 1963. Data are also given in this report on infant deaths from malignant neoplasms by sex.

597 ON THE EPIDEMIOLOGY OF CARCINOMA. I. THE GROWTH OF CANCER MORTALITY IN AUSTRIA. (Ger.) Denk, W. (Austrian Cancer Res. Inst., Vienna), H. Hansluwka and K. Karrer. Krebsforsch. 65(5):488-505, 1963.

Statistical studies of the cancer mortality of Austria in the last 40 yr. indicated a progressive increase in the number of deaths due to malignant neoplasms. In men the mortality increased at 55 yr. of age, in women at the 70th yr. The increase was definitely related to the position of the age group and the measure of statistical accuracy. With respect to these factors, the cancer mortality in Austria, when compared with other larger countries, was not so different as it seemed from the crude figures. There has been a genuine increase in carcinoma of the respiratory organs, especially in men, while gastric carcinoma has decreased.

63-1598 SOME ENDOCRINOLOGICAL REMARKS ON CANCER, NO. 4. DIABETIC GLUCOSE INTOLERANCE WITH REGARD TO CARCINOGENESIS. (Jap.) Shibusawa, K. Rinsho Fujinka Sanka (Clin. Gynec. Obstet.) 17(1):47-87, 1963.

The literature dealing with incidence of cancer in diabetic pts. is reviewed (75 references). A relationship has been recognized between diabetes mellitus or abnormal glucose metabolism and cancer, especially cancers of the uterine endometrium, the pancreas, and of the breast, as well as cancers of the common bile duct, mouth and lung. Besides cancer itself, there was also a relationship between abnormal glucose metabolism and precancerous conditions of the endometrium such as glandular hyperplasia or metaplastic and/or hyperplastic changes in the mammary duct, the pancreatic duct, and in the prostate.

63-1599 CYTOPLASMIC INCLUSION DISEASE COMPLICATING THE COURSE OF AN EOSINOPHILIC LEUKEMIA IN A 75 YEAR OLD MAN. (Fr.) Levillain, R. (Dept. Path. Anat., U. Besancon Natl. Sch. Med., France), G. H. Baufle, G. Pageaut and R. Lenys. Ann. Sci. Univ. Besancon, Med. (Ser. 2) (6):187-201, 1962.

At autopsy of a pt. dying of cardio-respiratory failure after unsuccessful treatment with prednisone (delta cortisone) and cyclophosphamide after presenting with a marked eosinophilia (59%), diffuse adenopathies, purpura and pruritus, it was found that a large number of cells in different areas of the body (thyroid, lymph nodes, stomach fundus mucosa, lungs (alveoli)) showed cytoplasmic inclusions which had all the characteristics of cytopathogenic viral inclusions. The author points out that the viral infection was probably concurrent with the blood disease.

63-1600 Pp. 312-431 in ANNUAL EPIDEMIOLOGICAL AND VITAL STATISTICS. 1960. (E. and Fr.) WHO, Geneva, 873 pp., 1963. \$20.00

In the volume covering the year 1960, the greater part devoted to malignant neoplasms deals with an analysis for each country of death by sex and age for selected sites. This is followed by a table giving death rates specific for sex and age, according to site, per 100,000 population. A third table gives death rates by sex for various sites, for other countries where more complete data was not available.

63-1601 KAPOSI'S SARCOMA IN NIGERIA. (E.) Maclean, C. M. U. (U. Coll. Hosp., Ibadan, Nigeria). Brit. J. Cancer 17(2):195-205, 1963.

While the geographic distribution of 63/68 cases of Kaposi's sarcoma in Nigeria is known, this, however, appears to reflect the available medical

services rather than real differences in incidence. Age distribution, where known, was, under 20 yr., 5; 20-29, 8; 30-39, 9; 40-49, 14; 50-59, 7; 60-64, 2. As to sex, 89% were males. Distribution according to site was: lower limbs, 47; upper limbs, 12; head and neck, 6; trunk, 5; penis and scrotum, 5; lymph nodes, 2; viscera, 1.

63-1602 THE EL PASO COUNTY MEDICAL SOCIETY FOLLOW-UP PROGRAM FOR CANCER. (E.) Hart, M. S. (415 E. Yandell Drive, El Paso, Tex.). *Southwest. Med.* 44(10):355-360, 1963.

The results of the program of the El Paso County Medical Society for the detection, treatment and follow-up of every cancer case living or treated in El Paso County has been reported. It covers 16,182 pts. who had 17,928 cancers diagnosed and treated for 18 yr. from 1944 through 1961. Incidence is given for Latin Americans (LTA; who comprise nearly half of the population) and others. Cancer of the lip is almost nonexistent among LTA females. According to the age-adjusted rates per 100,000 population for 1961, incidence for buccal cavity and pharynx for LTA females and "others" were 6.53 and 4.91, resp.; rates for breast cancer in females were 35.10 and 53.73, resp. Rates for intestines in females were 9.81 and 26.69, resp. Cancers of the rectum and urinary tract were higher among "others" than among LTA women. Among LTA males incidence was high in cancers of the buccal cavity and pharynx, the CNS, stomach and intestines. Incidence among "other" males was high in cancer of the lip, buccal cavity and pharynx, lung, intestines, urinary tract, prostate and the RES.

63-1603 CARCINOMA OF THE PENIS IN A CIRCUMCISED MAN. (E.) Kaufman, J. J. (Dept. Surg., U. California Sch. Med., Los Angeles) and T. H. Sternberg. *J. Urol.* 90(4):449-450, 1963.

The seventh case of penile carcinoma in a circumcised man is reported and the third in a Gentile circumcised at birth and the only case in this group in which there was no antecedent trauma. The pt. reported had a skin cancer diathesis (epidermoid carcinomas of the exposed surfaces) and it is likely that the penile lesion occurred as a result of his hereditary epidermal carcinogenic predisposition.

63-1604 THE BURKITT LYMPHOMA IN NATAL. A SIGNIFICANT MEDICAL TAIL. (Sic) (E.) Chapman, D. S. (Dept. Surg., U. Natal, Durban, S. Afr.) and T. Jenkins. *Med. Proc.* 9(16):320-331, 1963.

Detailed presentations are given of 5 cases of Burkitt lymphoma in children which occurred

during the past year in Natal, S. Africa. Three were boys, 2 Bantus aged 4 and 5, 1 a Zulu, aged 6; the others were a Thonga girl, aged 8 and a Bantu girl aged 3.5 yr. As far as could be determined, all 5 children had spent all their lives in villages situated at altitudes below 1,000 ft., where the mean temperature is above 60° F and the av. rainfall is above 20 inches. Most of the data would lend support to the climate dependence of the Burkitt lymphoma. The author does not believe the disease is new and suggests that many cases might have been missed in the past under other diagnoses.

63-1605 THE RELATIONSHIP BETWEEN LUNG CANCER AND CHRONIC BRONCHITIS. (E.) Campbell A. H. (Chest Dis. Repatriation Dept., Melbourne) and E. J. Lee. *Brit. J. Dis. Chest* 57(3):113-114, 1963.

For the purpose of this investigation, chronic bronchitis was defined as cough with sputum for most days of the year for at least two yr. The prevalence of chronic bronchitis in 99 pts. with lung cancer over the age of 50 yr. was found to be 74% compared with a prevalence of 45% amongst 166 controls, drawn from males over the age of 50 yr. admitted to the surgical and skin wards of the same hospital. The greater prevalence of chronic bronchitis amongst the lung cancer pts. compared with the controls was not due simply to greater tobacco consumption by the lung cancer group, since the increased prevalence is still evident when smoking habits are matched. The results suggest that chronic bronchitis may be a major, rather than an occasional, factor determining the genesis of lung cancer.

63-1606 PROBLEMS OF METHODOLOGY IN INVESTIGATION ON MALIGNANT TUMORS IN HUMAN POPULATION. (It.) Barberi, M. (Clin. Obstet. Gynec., U. Rome, Italy). *Ann. Sanita Pubblica* 24(2-3):223-281, 1963.

Methods for the study and evaluation of mortality and morbidity data in human populations are presented. Data are reported on international comparisons of general cancer incidence and on gynecological cancer in more detail. Italian data on mortality from cancer of the female reproductive system are analyzed according to geographic distribution (statistical regions), social and economic level (urban and rural districts) and ultimately to geographical characteristics (mountains, hills, and plains).

63-1607 MORBIDITY STATISTICS OF PLASMACYTOMA. INVESTIGATIONS ON INCIDENCE, SEX, AND AGE DISTRIBUTION AMONG 716 PLASMACYTOMAS, FROM THE TUMOR DISEASE STATISTICS OF THE GERMAN DEMOCRATIC REPUBLIC. (Ger.) Stobbe, H. (Dept. Hematol. 1st Med. Clin., U. Berlin) and G. P. Wildner. *Deutsch. Gesundheitsw.* 18(30):1318-1323, 1963.

ing the period 1953-1958, the annual number of cases of plasmacytoma reported increased; but whether this development is attributable to improved diagnosis, or to more careful reporting, or to an actual biological increase, must remain open question. Yet, the rate of new cases remains smaller than that of North America and the Scandinavian countries. Therefore, a further increase in plasmacytomas is to be expected in this country. The disease attacks males preponderantly, the ratio is 4 males:3 females; standardized values being 7.72 males and 6.00 females (per million new cases/yr.). The cause of the excess male incidence is not clear. Among 92% of the plasmacytomas occur after age 50. With advanced age, the incidence of new cases decreases sharply, due to as yet unknown reasons. It also occurs in chronic leukemias, the age distribution curve of which strongly resembles that of plasmacytoma.

608 DETERMINATION OF POLYCYCLIC HYDROCARBONS IN THE AIR. (Fr.) Rondia, D. Toxicol., U. Liege, Belgium). Arch. Med. Soc. 21(2):73-98, 1963.

In the large cities, the presence of smoke in the environment is a well known fact. The polycyclic hydrocarbons which are absorbed on particles which can be inhaled can have an influence on the number of pulmonary cancer which one observes. Described is a chromatographic method for the determination of tars which are extracted from this atmospheric smoke and the difficulties of spectrometric assay of polycyclic hydrocarbons. Attention is finally directed to the conditions

of sampling of the smoke (filtration on paper). See also CRA 1(3):#403, 1963. (Author summary)

63-1609 MALIGNANT LYMPHOMATA. AN EPIDEMIOLOGICAL STUDY. (Heb.) Frand, U. I. (Dept. Hemat., Tel-Hashomer Hosp., Israel) and B. Ramot. Harefuah (Tel-Aviv) 65(3):83-86, 1963.

A series of 399 cases of malignant lymphomata seen during 1955-1960 and classified as Hodgkin's disease, lymphosarcoma, reticulum-cell sarcoma and the undifferentiated type, were reviewed. A significantly higher incidence of malignant lymphomata in the younger age group (9-19 yr.) was found among Arabs and non-Ashkenazi Jews. A higher incidence of malignant lymphomata was found among Ashkenazi Jews over the age of 50. A higher incidence of the abdominal form of the disease was found among Arabs and non-Ashkenazi Jews and of the lymphadenopathic form among Ashkenazi Jews. The significance of these findings is not clear. (Author summary)

63-1610 RELATIONSHIP BETWEEN HERPES SIMPLEX AND LIP CARCINOMA-III. (E.) Kvasnička, A. (Oncol. Res. Inst., Bratislava, CSSR). Neoplasma 10(2):199-203, 1963.

There are analyzed 283 cancerous and 320 herpetic foci in the perioral region in men and women. It has been shown that occurrence of herpes simplex and carcinoma of the lips in both men and women is closely related as to degree. In the perioral region, in both sexes, cancer is frequent where the occurrence of herpes simplex is frequent and rarer where the occurrence of herpes simplex is rarer. In the skin area around the lips, malignant change develops less frequently in males than in females.

See also abstract nos.: 1423, 1426, 1430

- 63-1611 STUDIES ON THE MECHANISM OF IMMUNOLOGICAL ENHANCEMENT OF TUMOR HOMOGRAFTS. I. SPECIFICITY OF IMMUNOLOGICAL ENHANCEMENT. (E.) Möller, G. (Karolinska Inst. Sch. Med., Stockholm). J. Nat. Cancer Inst. 30(6):1153-1175, 1963.

Different mouse sarcomas were tested in systems designed to direct the antibodies against a number of antigenic components differentiating tumor and host, all belonging to the H-2 system. This was accomplished by variation of the specificity of the antiserum or the genotype of the recipients. All systems gave analogous results: a strong enhancing effect when the antibodies were directed against all tumor antigens foreign to the host, but no or diminished enhancement when only some of these antigens were covered by antibodies. Inhibition was directly related to the number or "strength" of the antigens remaining uncovered by antibodies. Passively transferred antibodies inhibited the humoral antibody response to tumor inoc. Antibody action was specific in this system too: passively transferred antibodies inhibited the immune response only against corresponding antigens, while other isoantigens on the same tumor cells still immunized efficiently. The pronounced specificity of the enhancing effect was incompatible with the hypotheses postulating antibody-induced alterations of tumor-cell characteristics, such as increased growth rate or increased resistance to the homograft reaction, but agreed with the assumption that antibodies interfere with the immunological relationship between tumor and host. (Author summary)

- 63-1612 STUDIES ON THE MECHANISM OF IMMUNOLOGICAL ENHANCEMENT OF TUMOR HOMOGRAFTS. II. EFFECT OF ISOANTIBODIES ON VARIOUS TUMOR CELLS. (E.) Möller, G. (Karolinska Inst. Sch. Med., Stockholm). J. Nat. Cancer Inst. 30(6):1177-1203, 1963.

Attempts were made to induce enhancement with tumors showing partial or full sensitivity to the cytotoxic action of H-2 antibodies. Partially sensitive tumors could be enhanced in H-2 systems. A completely sensitive leukemia could be enhanced in non-H-2 systems. It could not be demonstrated that antibodies stimulated tumor growth. On the contrary, inhibition was constant with several tumors and different test systems. Tumor cells exposed to antibodies for a short period *in vitro*, or a long time *in vivo*, did not change their transplantation characteristics to increased homotransplantability. Enhancement was obtained with tumor cells coated with antibodies in the absence of circulating antibodies in the hosts. Such antibody-coated cells were inferior to untreated cells in their ability to elicit the homograft reaction. It was concluded that antibodies did not change

tumor-cell characteristics, such as growth rate or resistance to the homograft reaction, but probably exerted their effect by an "afferent" or "efferent" inhibition of transplantation immunity and not by a "central" mechanism. Different doses of antibodies affected various tumors differently: large doses caused inhibition with some tumors and enhancement with others while smaller doses enhanced to various degrees. A possible explanation of the dose effect was advanced in terms of an "afferent" or "efferent" inhibition of the homograft reaction, and depended on the cytotoxic sensitivity of the tumor cells and their number of isoantigenic receptors. (Author summary)

- 63-1613 STUDIES ON THE MECHANISM OF IMMUNOLOGICAL ENHANCEMENT OF TUMOR HOMOGRAFTS. III. INTERACTION BETWEEN HUMORAL ISOANTIBODIES AND IMMUNE LYMPHOID CELLS. (E.) Möller, G. (Karolinska Inst. Sch. Med., Stockholm). J. Nat. Cancer Inst. 30(6):1205-1226, 1963.

Immunological enhancement was studied specifically to demonstrate the possible occurrence of "efferent" inhibition of transplantation immunity caused by humoral antibodies. Enhancement could be induced in preimmunized foreign recipients by treatment of tumor cells with antibodies *in vitro* before their inoc. Tumor cells coated with humoral isoantibodies had a lower capacity to absorb antibodies of the same specificity than untreated cells. Passive transfer of humoral antibodies into preimmunized recipients prevented an efficient secondary response. The experiments suggested that enhanced growth of antiserum-treated tumor cells in preimmunized recipients may be caused by a dual effect of antibodies, an "afferent" inhibition of transplantation immunity inhibiting the development of the secondary response and an "efferent" suppression of the homograft reaction protecting the tumor cells from destruction by the immune effector mechanisms. The protective effect of antibodies was studied. Tumor cells were mixed with antibodies and immune lymphoid cells and inoc. into foreign hosts or recipients which were compatible with the tumor cells and lymphoid cells. Antibodies antagonized the neutralizing effect of immune lymphoid cells efficiently in foreign recipients, caused partly by inhibition of the homograft reaction of the host itself and partly by protection of the tumor cells. Protection by humoral antibodies was also demonstrated in compatible recipients and, since the homograft reaction could not interfere, the effect of antibodies could be ascribed exclusively to "efferent" inhibition of transplantation immunity. (Author summary)

- 63-1614 STUDIES ON THE EFFECT OF HUMORAL ISOANTIBODIES ON TUMOR GROWTH. (E.)

Sjiler, G. (Karolinska Inst. Sch. Med., Stockholm). Acta Un. Int. Cancr. 19(1-2): 201-204, 1963.

See CRA 1(8):#1611; ibid., #1612; ibid., #1613, 1963.

63-1615 AETIOLOGY OF LEUKEMIAS. (E.) Kemp, N. H. (St. George's Hosp., London, W. 1), J. L. Stafford and R. Tanner. Lancet 195, 1963.

In investigations into primary bone marrow disease 5 pts. have been studied during the early stages of chronic myeloid leukemia. The first, studied as one of a series of pts. with polycythemia rubra vera, contained only Ph¹-positive cells in the bone marrow at a time when there was no clinical or hematological evidence of a leukemic process; the peripheral blood was then Ph¹-negative. Several mo. later immature granulocytes began to circulate and eventually the picture became typical of chronic myeloid leukemia when all the circulating leukocytes were Ph¹-negative. The 4 other pts. presented as diagnostic problems, with persistently raised WBC (24,000-110,000) and without any other evidence of leukemia. Some Ph¹-positive cells were found in the peripheral blood of all of these pts. Although the exact etiological significance of the Ph¹ chromosome in chronic myeloid leukemia remains to be determined, it is apparent that Ph¹-positive cells are present not only before the disease is clinically manifest but before there is any hematological evidence of the disease.

63-1616 TRANSPLANTATION OF LETTRE-EHRlich ASCITES TUMOR CELLS TREATED WITH GLYCERIN. (Ger.) Lónai, P. (Frederic Joliot-Radiol. Res. Inst., Budapest, Hungary), Antoni and E. J. Hidvégi. Zschr. Krebsforsch. (5):480-487, 1963.

After treatment of Lettré-Ehrlich ascites tumor cells with 35-80% glycerin, there is a considerable loss of RNA and protein; however, the content of DNA remains unaltered. In such damaged cells the cytoplasm is markedly reduced; in contrast, the structure of the nucleus resembles that of intact cells. When such altered cells are inoculated into mice, they produce ascites tumors which, as regards the survival rate of the animals, are more malignant than the original ascites tumors. The increased malignancy of the new tumors is directly proportional to the loss of RNA and protein from the original cells. (Author summary)

63-1617 RELATIONSHIP BETWEEN TUMOR GROWTH AND THROMBOKINASE ACTIVITY OF TUMOR TISSUE. (Ukr.) Ukolova, M. A. (Rostov State Res. Inst. Radiat. Oncol., RSFSR Min. Health,

USSR) and E. B. Kvakina. Fed. Proc. 22(3): 565-568, 1963.

The peripheral (growing) parts of Sarcomas M-1 and 45 possess much higher thrombokinase activity than the central (degenerating) parts. The level of the thrombokinase activity in the different parts of a fully developed tumor reflects the local relationship between growing and disintegrating tumor elements; as a rule, it is decreased in the more central parts of the tumor. The lower thrombokinase activity of Sarcoma M-1 as compared with Sarcoma 45 is associated with the earlier onset of necrosis in tissue of the Sarcoma M-1. The high thrombokinase content in the growing parts of the tumor at all stages of its development indicates an association with the processes of tumor growth and not with tissue destruction, which suggests that thrombokinase plays a part in the pathogenesis of the tumor. (Author summary)

63-1618 A MULTIVARIATE ANALYSIS OF SOME EXPERIMENTS IN TUMOR IMMUNITY. (E.) McHugh, R. B. (Dept. Path., U. Minnesota Sch. Med., Minneapolis), J. E. Faulkner and H. M. Hirsch. Folia Biol. (Praha) 9(3):171-176, 1963.

Young, inbred female C3H mice were injected repeatedly with preparations from spontaneous C3H mammary tumors plus Freund's adjuvant. The effect of these injections on the subsequent development of spontaneous mammary tumors was studied. The data, which had been analyzed previously by conventional statistical methods, were re-examined with a statistical approach of the multivariate type. This analysis yielded, in the present instance, inferences that were in quite close agreement with those presented earlier. In the present case, analysis by the multivariate technique confirmed that pretreatment with isologous mammary tumor tissue did not lead to a significant reduction in spontaneous mammary tumor incidence; did not delay age of tumor onset; nor prolong survival time following onset of tumors; but led, on the contrary, to a significant reduction in the age at which spontaneous mammary tumors occurred. (Author summary)

63-1619 OVARIAN TUMORIGENESIS FOLLOWING GENIC DELETION OF GERM CELLS IN HYBRID MICE. (E.) Murphy, E. D. (Roscoe B. Jackson Mem. Lab., Bar Harbor, Maine) and E. S. Russell. Acta Un. Int. Cancr. 19(3-4):779-782, 1963.

Abnormal genes of the W-series produce a marked deficiency in the number of germ cells incorporated in developing ovaries. The very few primary follicles that develop disappear during the first mo. of life. Serial sections of ovaries, adrenals, and pituitary gland, and sample sections of the uterus and vagina were studied in 77 (C57BL/6 x C3H/He)F₁ hybrid sterile females

of genotypes W^xW^v and W^jW^v , along with 68 heterozygous and normal littermate controls. The sterile ovaries, lacking ova and follicles at 2 mo. of age, progressed through stages of tumorigenesis classified as tubular adenomas, complex tubular adenomas, and finally granulosa-cell tumors and luteomas. From 6 mo. of age, the complex tubular adenomas demonstrated an almost straight-line exponential increase in volume. There was evidence of continuing estrogenic stimulation of the reproductive tract after 4 mo. of age. The method of genic deletion of ova has advantages of cytological specificity, and spontaneity, and offers a new approach to the problems of ovarian tumorigenesis. (Author summary)

- 63-1620 EFFECTS ON CELL GROWTH BY A SERUM FRACTION FROM PATIENTS WITH CENTRAL NERVOUS SYSTEM NEOPLASMS. (E.) Wilkins, R. H. (NCI, Bethesda). *J. Neuropath. Exp. Neurol.* 22(4):677-694, 1963.

An ether-soluble, saline-insoluble fraction was extracted from the sera of 100 pts. and its effects on cell growth were measured by using the test system of the regenerating rat liver. This fraction from 36 pts. with malignant central nervous system neoplasms and 5 with carcinoma of the uterine cervix was found to significantly stimulate liver regeneration, an effect not related to the amount of tumor present or its degree of malignancy. The same fraction from 19 pts. with benign CNS neoplasms and 40 pts. with no neoplasms was found to significantly inhibit liver regeneration. (Author summary)

- 63-1621 GROWTH OF THE MAST-CELL TUMOUR P.815 IN THYMECTOMISED MICE. (E.) Ross, P. W. (Dept. Bact. Path., U. Aberdeen, Scotland) and P. V. Best. *Lancet* 2:611-612, 1963.

C3H mice thymectomized within 24 hr. of birth became susceptible to the P.815 mast-cell tumor which will normally grow only in DBA/2 mice and a few F1 hybrids of DBA/2. The tumor in the thymectomized C3H animals showed more necrosis than in the normal DBA/2 host. (Author summary)

- 63-1622 EXPERIMENTAL TRACHEOBRONCHIAL CARCINOMA. (E.) Staub, E. W., B. Mills, G. M. Hass, and E. J. Beattie, Jr. *Proc. Inst. Med. Chicago* 24(11):298, 1963.

In a study of experimental tracheobronchial carcinoma, two groups of healthy mongrel dogs were used. In Group I a segment of cervical trachea was surgically reversed. As the cilia of the reversed segment now beat in the caudad direction, a "mucous block" occurred at the caudad anastomosis. In Group II no surgical procedure was performed. Eleven dogs in each group were treated with 9,10-dimethyl-1,2-benzanthracene (DMBA), instilled weekly into

the right mainstem bronchus. The total dose administered in one year was 100-110 mg for each animal. All dogs in Group I have died or been sacrificed and studied. Histologically proven malignancy resembling human bronchogenic carcinoma was found in three dogs as follows: two tumors occurred at the caudad anastomosis, one at the cephalad anastomosis, and, in one dog with a tumor at the caudad anastomosis, microscopic tumor was found in the right mainstem bronchus. None of the dogs in Group II have developed malignancy after a similar period of time and DMBA dosage.

- 63-1623 STUDIES OF AN INJURY-INDUCED GROWTH IN THE FROG LENS. (E.) Rafferty, N. S. (Dept. Anat., Johns Hopkins U. Sch. Med., Baltimore, Md.). *Anat. Rec.* 146(4):299-312, 1963.

A tumor-like growth in the lens of *Rana pipiens* occurs following mechanical injury to the lens. The frequency of occurrence and size of the growth are roughly dependent on the extent of the injury inflicted. The growth first appears 4 days after wounding, grows actively for 3 wk and usually begins to regress after a mo. The cells of the growth appear to originate by proliferation of the lens epithelial cells surrounding the wound which grow into and actively invade the lens fibers. The lens growth was not transplantable either homologously into the anterior eye chamber nor isologously in a s.c. site. Protein and 3 dehydrogenases (lactic, malic, and glucose-6-phosphate) were similar for normal and abnormal lenses. Whether a true tumor or hyperplasia, the frog lens exhibits an unique reaction to the injury stimulus which is not found in mammal (man, rabbit, mouse). (Author summary)

- 63-1624 EFFECTS OF MALIGNANT EFFUSIONS ON THE MITOTIC INDEX OF L STRAIN MOUSE CELLS GROWN IN TISSUE CULTURE. (E.) Hrushovetz, S. B. (Cancer Res. Inst., U. Saskatchewan, Saskatoon, Canada) and M. H. Ewaniuk. *Canad. Med. Assn. J.* 89(18):926-932, 1963.

By employing a clone of L strain mouse fibroblasts (L_E) which does not exhibit cell clumping and lysis (cytolytic antibody reaction), it was possible to screen for the presence of growth-regulating factors in human sera and effusions, exclusive of an antigen-antibody reaction. Under conditions of the test a mitotic index greater than 20% indicated the presence of a growth-promoting factor. A total of 11 pleural effusions was tested. A growth-promoting factor was found in 4/8 malignant effusions, while none of the three nonmalignant effusions or the one sample of human umbilical cord serum possessed such a factor. Overnight storage of the unfiltered effusions at 5° C resulted in complete loss of the growth-promoting activity. (Author summary)

3-1625 THE ANTIGENIC STRUCTURE OF RAT SARCOMAS INDUCED BY HUMAN SARCOMA TISSUE EXTRACTS. (E.) Bashkayev, I. S. (Hertzen State Inst. Oncol., Moscow) and A. I. Ageenko. *Czechoslovak Biol.* (Praha) 9(3):177-180, 1963.

tumor tissue antigen not present in normal rat organs and muscle was found in rat sarcomas induced by human sarcoma tissue extracts. This antigen, whose electrophoretic mobility was similar to that of serum globulins, was maintained in transplantation of the induced sarcoma in rats. The rat tumor tissue antigen is serologically related to the tumor tissue antigen of the human sarcoma. (Author summary)

4-1626 EFFECTS OF SPECIFIC GENES OF THE MOUSE ON NORMAL GROWTH AND ON THE OCCURRENCE OF TUMORS. (E.) Heston, W. E. (NCI, Bethesda). *Int. J. Cancer*. 19(3-4):776-778, 1963.

total of 12 specific genes of the mouse presenting seven linkage groups have been shown to be associated with either an increase or decrease in occurrence of one or more kinds of tumors. Most of these genes also have a comparable effect on normal growth. The lethal yellow gene (AY) that increases amount of adipose tissue and also increases muscular and skeletal growth, increases susceptibility to pulmonary tumors, hepatomas, and mammary tumors. The recessive obesity gene (ob) that greatly increases adipose tissue but slightly reduces muscular and skeletal growth, increases susceptibility to hepatomas but decreases susceptibility to pulmonary and mammary gland tumors. (See also CRA 1(6):#1106, 1963.) (Author summary)

5-1627 THE IMMUNOLOGICAL THEORY OF CANCER. (E.) Green, H. N. (Dept. Exp. Path., Leeds Sch. Med., England) and H. M. Anthony. *Immunologist* 190:705-714, 1963.

characterization and function of tissue specific antigens (TSA) and their absence in chemically induced neoplasms are reviewed and discussed (17 references). Preliminary results of an experiment designed to assign a specific role to TSA in chemical carcinogenesis are also reported. Antisera prepared by injecting normal liver microsomal fraction M (containing cytochrome P-450) or microsomal fraction M from livers of rats injected with amino-azo dye 48 hr. before, were carefully absorbed to eliminate isoantigenic sites. In a small preliminary experiment, both rats injected with antiserum to microsomes of normal livers died 8 and 10 mo. after cessation of treatment, both with abdominal tumors. Rats injected with antiserum to dye-conjugated microsomes showed no abnormality when killed after 10 mo.

63-1628 SUCCESSFUL RE-INTRODUCTION OF THE MURPHY-STURM LYMPHOSARCOMA AFTER METHYLCELLULOSE-INDUCED REGRESSION OF THIS TUMOUR IN RATS. (E.) Lazar, A. W. (Dept. Path., U. Chicago Hosp. Clin.) and D. E. C. Lazar. *Nature (London)* 199:48-50, 1963.

Murphy-Sturm lymphosarcoma was injected s.c. into the right scapula of groups of Sprague-Dawley rats 300-360 g in wt. In a first passage tumors became established in all 26 control rats and 40 rats treated with methylcellulose (MCL, "Methocel 400 CPS", 2.5%, 2 ml 3x/wk. for life). After 11 days growth, regressions began in 38/40 of the MCL group and 6/26 untreated rats. After 40 days from the first transplantation, a second was made (into the left scapula). The tumor took in all 20 of a new control group from the same shipment; the tumor killed 17, while 3 rats showed regression. A second transplantation of 12/38 MCL rats which showed regression resulted in 9/12 tumors which grew for 10 days and then completely regressed. None of the 6 control rats which had shown spontaneous regression developed tumors when transplanted a second time. All survivors were transplanted again (into the lumbar area) 40 days after the second transplantation, along with 20 new, unused controls. Tumors again grew in all 20 controls, killed 16 while 4 showed regression. None of the other inoc. rats had detectable tumors after 20 days at which time they were killed for study.

63-1629 EFFECT OF ORGAN SPECIFIC SERA ON THE LOCALIZATION OF METASTASES FROM THE BROWN-PEARCE TUMOR. (E.) Maiskii, I. N. (Inst. Exp. Biol., Acad. Med. Sci. USSR, Moscow). *Biull. Eksp. Biol. Med. (Eng.)* 54(7):784-786, 1963.

Antisera (prepared by immunization of sheep with different tissues of the rabbit) were administered to groups of chinchilla rabbits in either large doses (2 ml x 15 during 1 day, injected begun 10 days before inoculation with Brown-Pearce tumor) or small doses (0.2 ml x 5 over a 3-day period, injected begun 3 days after tumor inoculation). All animals were killed 24 days after tumor inoculation. The mean number of metastases in the organ investigated in rabbits given anti-lung serum (large, small dose, control without serum) was - 1.7, 0, 0; in those given anti-liver serum - 50.1, 19.2, 29.7; in those given anti-kidney serum - 24.5, 2.5, 10.5. When normal serum was injected, comparable results were: lungs - 0.2, 14.2 -; liver - 22, 40.2, 29.7; kidney - 17.5, 18.5, 10.5. There thus appears to be a definite localization of metastases in those organs to which the anti-organ serum had been administered.

63-1630 CHROMOSOMAL ABNORMALITIES IN CHILDREN WITH ACUTE LEUKEMIA. (E., Abstract)

Weinstein, E. D. (Children's Hosp. Res. Found., Cincinnati, Ohio) and A. W. Weinstein. J. Pediat. 63(3):473-474, 1963.

When studies were made of 6 cases of acute leukemia, 5 had a normal chromosome number and karyotype. The 6th pt., a child with myeloblastic leukemia, had 47 chromosomes in 75% of her blood cells. The extra chromosome was consistently in the 6-12 group. A 7th pt. recently was studied (also with acute myeloblastic leukemia) and was found to have a similar chromosomal abnormality.

63-1631 CARCINOGENICITY OF PREHEATED FATS. (E.) Zaldivar, R. S. d. (Dept. Biol., U. Chile, Santiago). Nature (London) 199:1300-1301, 1963.

Fat from guinea pigs which was preheated to 360°-365°C for 30 min. was given by inj. to groups of 6 to 11 female guinea pigs (initial av. wt. 470 g) into the wall of the antrum and fundus in doses of 0.05 ml. One group sacrificed at 150 days received 0.1 ml into the wall of the antrum only. After periods from 16 to 240 days, 18/36 animals had developed gastric lesions (mainly focal hyperplasia of the epithelium, diverticula, and glandular infiltration of the submucosa through perforation of the muscularis mucosae). No such lesions were seen in groups of 6 to 9 (total 28) control animals given ether-extracted fat and observed from 17 to 240 days. The lesions

seen in the experimental groups at the present time are not classed as precancerous, but some of them are similar to those induced by 20-methyl-cholanthrene.

63-1632 ALKALINE PHOSPHATASE ACTIVITY AND CHROMOSOME VARIATION IN HUMAN CELLS IN CULTURE. (E.) De Carli, L. (Inst. Genet., U. Pavia, Italy), J. J. Maio and F. Nuzzo. J. Nat. Cancer Inst. 31(6):1501-1509, 1963.

A detailed chromosomal analysis of a heteroploid strain of human cultured cells with very high alkaline phosphatase activity and of enzyme-deficient lines derived from the same strain indicates that the reduction in enzyme activity may be associated with a loss of 7 to 8 chromosomes. Furthermore, the chromosome losses in the deficient lines were not distributed randomly over the various groups, but were most pronounced in groups IV (long acrocentrics) and VII (short acrocentrics). Group VII showed the greatest loss: the chromosome number was at least halved with respect to the parental strain. However, the differences in specific alkaline phosphatase activities between the parental strain and the deficient lines were nearly 1000-fold. Therefore there apparently is no linearity between alkaline phosphatase activity and chromosomal dose in these cells. The present findings agree with the claim that short acrocentric chromosomes may be carriers of genes controlling alkaline phosphatase activity in human cells.

ERRATA

1(2):#172, 1963. Line 18 of text, change Gritsiute to Gričiūte.

1(2):#337, 1963. Line 12, change sentence starting: "Basal-cell carcinoma was more prevalent....." to "The relative frequency of basal cell carcinoma to squamous carcinoma was higher in Australia than in Britain, but is greater in New Zealand than in Australia. The most frequent site of basal cell carcinoma was on the head and neck."

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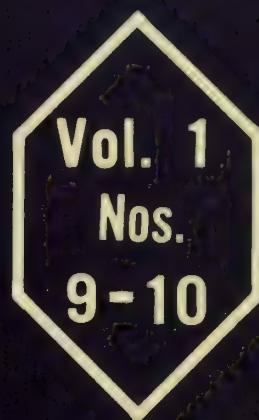
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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration(s)	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health, USA
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit(s)
e.g.	for example	ppm	parts per million
FFU	focus forming unit(s)	pt.(s)	patient(s)
g	gram(s)	RBC	red blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
ID ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution(s)
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit(s)
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose(s)	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

1633 AN EXPERIMENTAL CONTRIBUTION TO TOBACCO SMOKE CARCINOGENESIS. (Ger.) Wynder, L. (Sloan-Kettering Inst. Cancer Res., New York) and D. Hoffmann. Deutsch. Med. Wschr. (13):623-628, 1963.

This review assembles in brief the experimental evidence gathered from publications by the authors and by others, showing: (1) the induction of animal tumors by tobacco smoke condensate; (2) the fractions of such condensates which are carcinogenic, and their relative activities of polycyclic and heterocyclic hydrocarbons and carcinogenic phenols and terpenes; and (3) the possible decrease of the carcinogenic content of tobacco smoke by additives which promote complete combustion, by selection of tobacco types with smallest benzo(a)pyrene and phenol content, and by selective filtration. (38 references)

1634 BENIGN AND MALIGNANT TUMORS OF THE LIVER. (Sp.) Nasio, J. (Internatl. h. Gastroenterol., Cordoba, Spain) and E. Galindez. Sem. Med. (B. Air.) 122(17):604, 1963.

In a previous report the authors analyzed data from the world literature. In the present review the data are discussed briefly, including frequency at autopsy, relation to race, to cirrhosis, to age, and to sex. There is a distinction on etiology, one on experimentally induced tumors, and a discussion of benign tumors. (7 references)

1635 OCCUPATIONAL CANCER AS ONE OF CHRONIC INDUSTRIAL POISONINGS. (Jap.) Kikuchi, K. (Dept. Prevent. Med. Public Health, Keio Sch. Med., Japan). Sogo Igaku (Med.) 1(1):86-90, 1963.

A review is presented of the relationship between exposure to various types of industrial poisons and cancer. (7 references)

1636 THE PRESENT POSITION OF EXPERIMENTAL INVESTIGATIONS INTO THE AETIOLOGY OF BLADDER CANCER. (E.) Pyrah, L. N. (Dept. Cancer Res., U. Leeds, England) and J. Clayson. S. Afr. Med. J. 37(30):788-791, 1963.

Recent studies on bladder carcinogens are reviewed and the metabolism of carcinogenic amines is discussed in the light of the two principal theories of industrial bladder carcinogenesis: conversion to either ortho hydroxamine or to an N-hydroxylamine. It is also mentioned that recently G. M. Bonser tried to distinguish between the two theories by testing 2-naphthyl-N-hydroxylamine and the phosphate ester of

2-amino-1-naphthol (thought to be the active form of 2-amino-1-naphthol). However results did not decide between the two hypotheses, and instead suggest that there may be truth in both mechanisms. (18 references)

64-1637 MODERN MEDICINE VERSUS CIGARETTES. (Por.) Blundi, E. (Fac. Med., U. Rio de Janeiro, Brazil). Rev. Brasil. Anest. 20(5):274-277, 1963.

A brief review of the evidence linking cigarette smoking to lung cancer, with comments on the attitude of various official agencies toward cigarette advertisements. The author points out that in 1958 he demonstrated a firm correlation between cigarette smoking, chronic bronchitis and pulmonary emphysema. (17 references)

64-1638 NEW RESULTS OF LEUKEMIA RESEARCH. (Ger.) Hunstein, W. (Clin. Med., Albert-Ludwigs-U., Freiburg, Germany). Med. Klin. 58(28):1141-1145, 1963.

A review is presented of a number of exogenous factors operative in experimental, as well as in clinical leukemia, and the interplay of endogenous factors. At the present time the cause and pathogenesis of leukemia remains unknown. The role of the chromosomal abnormalities in leukemia is also discussed. (74 references)

64-1639 VIRUSES AND TUMORS. RECENT FINDINGS ON VIRAL AGENTS DEMONSTRATED IN ANIMAL TUMORS. (It.) Albano, A. (Inst. Hygiene, Virol. Ctr., U. Milan, Italy). Boll. Ist. Sieroter. Milan 41(11-12):560-584, 1962.

After a brief review of carcinogenic viruses in fowl, mice and rabbits, possible mechanisms of viral carcinogenesis in humans are discussed. The author favors the theory of persistent latent infection which becomes established on production of antibodies or of an interferon-like substance, thus blocking the cytopathogenic action of the virus. (268 references)

64-1640 GENETIC ASPECTS OF THE RELATIONSHIP BETWEEN VIRUSES AND TUMORS. (E.) Klein, G. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm). Pp. 480-500 in Recent Progress in Microbiology. Symposia Held at the VIII International Congress for Microbiology, Montreal, 1962. Gibbons, N. E. (Ed.). U. Toronto Press, Canada, 1963.

In a thoughtful and thorough discussion the author considers three points: interaction between oncogenic virus and target cell; interaction between virus and animal host; and relationship

between virus-induced tumor cell and host. The influence of natural genetic variation or of virus-induced genetic changes on the properties of various systems are examined in a few well studied cases. The author considers mechanisms of carcinogenesis where viruses play direct and indirect roles, e.g., initiating, promoting or contributing to tumor progression. The role of the viral genome in the determination of neoplastic phenotype is examined, with special emphasis on examples from antigenic tumors. An examination of bacterial systems suggests that in the polyoma system at least, close analogies may be found between the neoplastic transformation and lysogenic conversion in *Salmonella*. Other examples of cellular phenotypic changes after tumor virus infection are reviewed, some of which may be an expression of the neoplastic character of the cells, rather than due to direct viral action. Aside from theoretical significance, studies of virus-tumor antigenicity are thought to have prophylactic importance, and a delay in time of tumor appearance is said to have followed non-specific bolstering of host immunologic response. (76 references)

- 64-1641 PROBLEMS RELATED TO THE DEMONSTRATION OF ONCOGENIC VIRUS BY MEANS OF THE ELECTRON MICROSCOPE. (Fr.) Bernhard, W. (Inst. Cancer Res., Villejuif (Seine), France). Pp. 467-479 in *Recent Progress in Microbiology*. Symposia Held at the VIII International Congress for Microbiology, Montreal, 1962. Gibbons, N. E. (Ed.). U. Toronto Press, Canada, 1963.

After a brief review of methods used for the demonstration of a viral etiology for cancer in experimental animals, emphasis is placed on work by the author and by others leading to the demonstration and morphologic characterization of many known oncogenic viruses by electron microscopy. At the present time ideal conditions for electron microscopic demonstration of tumor viruses have been in tumors which show a marked increase in viral titer on *in vitro* culture, and in some tumors appearing with high spontaneous frequency in pure mouse lines (such as mammary tumors). On the other hand a large number of tumors, thought to be of viral origin, fail to show virus particles on electron microscopy. Search for cellular lesions has demonstrated nuclear lesions (especially in Hodgkin's cells and in human lymphosarcomas) consisting of dense nuclear bodies, abnormal nucleoli and granulation. Similar lesions have been observed in some acute viral infections, in Rous sarcoma, and in the early stages of polyoma or SV40 carcinogenesis. Interpretation of such results remains cautious, as is the interpretation of electron microscopically demonstrable viral particles in human tumors. However, it is pointed out that the recent finding of adenovirus type 12 and SV40 as carcinogenic agents could be interpreted as a demonstration of the

importance of presumably endogenous nontumor viruses in tissues. (66 references)

- 64-1642 ROLE OF INFECTIOUS AGENTS IN THE PATHOGENESIS OF NEOPLASIA. (E.) Horsfall, F. L., Jr. (Sloan-Kettering Inst. Cancer Res., New York). Pp. 458-466 in *Recent Progress in Microbiology*. Symposia Held at the VIII International Congress for Microbiology, Montreal, 1962. Gibbons, N. E. (Ed.). U. Toronto Press, Canada, 1963.

A brief presentation and discussion is given of the development of viral carcinogenesis. Possible mechanisms of carcinogenicity are discussed and comparisons are made between classical animal viruses or virulent bacteriophages, and temperate bacteriophages and tumor viruses. An important consequence of the phenomenon is that cancer cells resulting from the effects of certain viruses continue to produce daughter cells with neoplastic features, presenting heritable properties similar to those of classical mutations. (42 references)

- 64-1643 HOST-TUMOR ANTAGONISM. XXXIII. CANCER IMMUNITY--A REVIEW AND AN ANALYSIS OF SOME FACTORS IN HOST RESISTANCE TO CANCER. (E.) Pelner, L. (Swedish Hosp. Brooklyn, New York). *J. Am. Geriatr. Soc.* 11(9):843-883, 1963.

This review and analysis covers some of the early and recent research which attempts to prove tumor immunity by the presence of antibodies. The early attempts of Lumsden to demonstrate tumor immunity seem to be fully substantiated by recent work--although the antibodies may be in the cells rather than in the serum. (133 references)

- 64-1644 CYTOCHEMICAL INVESTIGATIONS ON NUCLEIC ACIDS OF TUMORS AND VIRUS INFECTIONS. (Ger.) Leuchtenberger, C. (Swiss Fed. Inst. Tech., Inst. Gen. Bot., Zurich) and R. Leuchtenberger. *Oncologia (Basel)* 16(3): 255-266, 1963.

Microspectrophotometric analyses of DNA and RNA content of normal, neoplastic, and virus-infected cells are reviewed and discussed. Neoplastic cells contain an increased and variable amounts of DNA as opposed to the constant amounts in normal cells; a local tumor may affect the DNA metabolism of the entire organism. Autopsies of tumor pts. and sections of mice with tumors showed increased and variable amounts of DNA in the liver. DNA from mouse tumors inj. i.p. into normal mice caused an increase in DNA content of their liver; a similar inj. of DNA from normal organs caused no increase in liver DNA. Virus infections are classified and tabulated according to the 2 possible effects. Effect 1: an intimate virus-host cell relationship (virus

rs cell) where virus multiplication leads to cell death; depending on the virus type, intracellular DNA or RNA is markedly increased. Effect II = absence of intimate virus-cell relationship (type of physical attachment uncertain), but the end effect of the relationship is cell proliferation or tumor formation; the cell DNA and RNA are massively increased. Conditions which may decide whether Effect I or Effect II takes place depend on a virus-host relationship. (21 references)

64-1645 ONCOGENIC VIRUSES (WITH PARTICULAR REFERENCE TO MOUSE LEUKAEMIA). (E.) Jost, A. (VA Hosp., Bronx, New York). Ann. Coll. Surg. Eng. 33(2):67-78, 1963.

A review of experimental transmission of viruses by filtrates, with special attention to leukemia, the author discusses various factors complicating study of viral carcinogenesis. Included are descriptions of the role of the thymus in viral leukemogenesis in C3H mice and in rats, the detection of latent leukemia viruses in transplanted mouse tumors, the stimulating effect of radiation on leukemia viruses and a discussion of polyoma virus, of adenoviruses type 12 and 18. A hypothesis is presented, to account for all carcinogenesis by a unitary viral theory. All cancers could be due to transmission of a latent agent, activated in a few members by a variety of probably nonspecific factors including radiation and chemical or hormonal factors. Recent observations on the oncogenic potentials of viruses such as SV40 and adenoviruses type 12 and 18 suggest that a virus is completely latent, or produce only minor effects in one species, while capable of oncogenesis in another. (47 references)

64-1646 HORMONES AND TERATOGENESIS. (Fr.) Jost, A. Pp. 35-47 in Effects of Hormones on the Foetus. Vol. I. Proc. European Study Drug Toxicity and Proc. Symp. in January 3, 1963. Internatl. Congress. Excerpta Med. Found. (Publ.), Amsterdam, 1963.

Effect of various hormones on fetal development is reviewed briefly. Among possibly teratogenic hormones or hormonal procedures are administration of antithyroid hormones to pregnant rats or of estrogens, testosterone and especially of synthetic progestones and corticoids. The author concludes that the period of evaluation of the teratogenic effects of hormones should be extended until the fetus has reached adulthood, and that studies should cover a larger group of species, since differential activities of possible clinical significance have been recorded among various laboratory animals. (46 references)

64-1647 RECENT FINDINGS ON THE VIRUSES OF AVIAN LEUKEMIAS. (Fr.) Brion, A. and M. Fontaine. Rev. Path. Gen. (746):317-331, 1963.

A review and discussion is presented of recent findings concerning virus-induced leukemias affecting poultry. Myeloblastosis virus may be detected using electron microscopy; it may be assayed chemically, since it causes hydrolysis of ATP; it embodies a "virulence antigen", "a normal chicken tissue antigen" and a "Forssman antigen", and it may originate from mitochondria in myeloblasts. The erythroblastosis virus does not hydrolyze ATP and lacks the Forssman antigen. (No references)

64-1648 GUIDES TO STUDIES OF VIRAL ETIOLOGY OF NEOPLASIA. (E.) Manaker, R. A. (NCI, Bethesda). Milit. Med. 128(9):881-887, 1963.

Citing work from his own laboratory and from the literature, observations have been presented that outline some characteristics of animal tumor viruses. Each agent has its own peculiarities, and a rigid protocol for future investigation cannot be defined. Careful consideration must be given to the choice of animal hosts or culture cell strains, to provision for the influence of inhibitors, and to the role of initiating dose in oncogenesis. In programs involving higher animals, the problems become increasingly difficult, but may not be insurmountable as more information becomes available from our animal models. (20 references) (Author summary)

64-1649 THE NUCLEUS OF THE CANCER CELL. A HISTORICAL REVIEW. (E.) Koller, P. C. (Roy. Cancer Hosp., London). Exp. Cell Res. Suppl. 9:3-14, 1963.

A review is presented of the role of the nucleus, from both the histological and cytochemical point of view, in the identification of cancer cells and in the detection of changes which are indicative of malignant transformation. (50 references)

64-1650 THE FINE STRUCTURE OF THE CANCER CELL NUCLEUS. (E.) Bernhard, W. (Res. Inst. Cancer, Villejuif (Seine), France) and N. G. Granboulan. Exp. Cell Res. (Suppl.) 9:19-53, 1963.

A discussion and review of the role of electron microscopy in the analysis of ultrastructural changes in the nuclei of cancer cells is presented. In the study of carcinogenesis, it is felt that only in *in vitro* systems can primary and secondary lesions be distinguished. The transformation of normal into malignant cells induced by an oncogenic virus in tissue culture is proposed as an experimental model for parallel

biochemical, structural and physiological analysis. (For some related studies, see CRA 1(2):#245; ibid., (6):#1134, 1963.) (57 references)

64-1651 CHROMOSOMES AND LEUKEMIA. (Sp.)
Moncada Lorenzo, E. (Fac. Med. Gen.
Stud., Navarre, Spain). Rev. Clin. Esp. 88(6):
398-403, 1963.

A review is presented of the significance of chromosomal aberrations in human leukemia. (44 references)

64-1652 CONVERSION OF CELLS BY AVIAN MYELOBLASTOSIS VIRUS. (E.) Baluda, M. A.
Pp. 118-137 in Perspectives in Virology III.
The Gustav Stern Symposium. Pollard, M. (Ed.).
Hoebner Med. Div. Harper & Row, Publ., Inc.,
New York, 292 pp., 1963.

A review is presented of various in vivo and in vitro studies which show that avian myeloblastosis virus can induce differentiation and unrestricted proliferation of some specific cell types. Also discussed are the antigenic changes which are the result of infection, and which may cause the host to react (see also CRA 1(2):#267, 1963). (11 references)

64-1653 TERATOGENIC AGENTS AND CONGENITAL MALFORMATIONS. (E.) Cohlan, S. Q.
(Dept. Pediat., New York U. Med. Ctr., N. Y.).
J. Pediat. 63(4):650-659, 1963.

Among the drugs discussed in this review are thalidomide, endocrine preparations, cytotoxic and metabolic agents and tolbutamide. Also discussed is the role of maternal infection and X-irradiation; presentation of the current principles of teratology conclude the paper. (58 references)

64-1654 THE ROLE OF VIRUSES IN CANCER. (E.)
Rowson, K. E. K. (Cancer Res. Dept.,
London Hosp. Med. Coll., E.1). Guy Hosp. Rep.
112(3):456-478, 1963.

A review previously abstracted as CRA 1(1):#31, 1963, but with some additional material on SV40, adenovirus and leukemogenic viruses. (133 references)

64-1655 ON THE CANCEROGENIC ACTIVITY OF SOME MEDICINAL SUBSTANCES. (BASED ON EXPERIMENTAL DATA.) (Rus.) Saliamon, L. S. (Inst. Oncol., Acad. Med. Sci. USSR, Leningrad). Vop. Onkol. 9(11):22-25, 1963.

The paper deals with the data from literature concerning the cancerogenic activity of contraceptives, isonicotinic acid amide, chlorpromazine

and some other medicinal substances. The author discusses the necessity of controlling their use and of testing the drugs supposed to possess cancerogenic activity. (15 references) (Author's summary)

64-1656 THE DIFFERENTIAL DIAGNOSIS BETWEEN VIRUS AND CYTOPLASMIC PARTICLES OF A DIFFERENT NATURE. THE PROBLEM SEEN IN THE COURSE OF THE ELECTRON MICROSCOPE STUDY OF TUMORS. (E.) Haguénau, F. (Lab. Exp. Med., Coll. France, Paris) and K. H. Hollmann: Bull. Assn. Franc. Cancer 50(1):29-48, 1963.

A brief review describing the different aspects in electron microscopy taken by intracellular viruses and particles that are virus-like in appearance in mammalian tumors. (18 references)

64-1657 AFLATOXICOSIS IN ANIMALS CAUSED BY A MYCOTOXIN PRESENT IN SOME BATCHES OF PEANUTS (ARACHIS HYPOGAEA). (E.) Allcroft, R. (Centl. Vet. Lab., Weybridge, Surrey, England) and G. Lewis. Biochem. J. 88(3):58P, 1963.

Briefly reviewed are distribution, susceptibility, and type of lesions found in animals (turkey poults, ducklings, pigs, calves, guinea pigs and ferrets) fed peanuts and peanut meal containing aflatoxin, a toxic metabolite of Aspergillus flavus Link. Since the disease has been known probably for 12 yr. in guinea pigs fed peanut meal, it is concluded that it affected other animals, but was incorrectly diagnosed. (6 references)

64-1658 THE TRUE ORIGIN OF CANCER CELLS. (S) Martino Savino, F. Rev. Clin. Esp. 89(5):282-287, 1963.

Carcinogenesis is interpreted as due to the increased exposure of cells to glucose in the absence of oxygen (due to a lower solubility of oxygen in plasma and intracellular fluids) leading to a fermentative, instead of an oxidative type of metabolism. Actual carcinogenesis is thought to be secondary to excessive lactic acid production leading to decreased intracellular pH and consequently to cross-linking of the DNA. The initiating mechanism is thought to be anoxia accompanied by prevention of physiologic reaction hyperemia (such as could be found in aged individuals with arteriosclerosis, or in children with insufficient vascularization), following cellular stimulation by irritants or hormones. In rabbits the author obtained a canceroid histologic appearance or hyperplasia within 7 days by the inj. of 22-methylcholanthrene (0.1 ml of a 1% suspension in mineral oil in the ear) followed by gentle continuous mechanical compression of the inj. sites. The author believes that tumor tissue in vivo exhibits absolute anoxia, and that no oxygen evolves from tumor cells in tissue culture. (16 references)

659 CARCINOGENESIS, A BIOLOGICAL PROCESS. (E.) Laws, J. O. (Dept. Exp. Path., Leeds Sch. Med., England). Guy Hosp. Rep. 3(3):449-455, 1963.

by cancer changes in tissues, especially treatment with chemical carcinogens are reviewed. Emphasis is placed on changes in the organization and especially in the loss of cell adhesion observed in many cancer cells. (References)

660 THYMIC MASTOCYTES AND THE RELATIONSHIP OF THE DEFENSE MECHANISMS OF THE ORGANISM TO CANCER PATHOGENESIS. (Fr.) Klein, R. (Ec. Clin., Broca Hosp., Paris). C.R. Soc. Sci. (Paris) 157(4):718-720, 1963.

Theory of carcinogenesis is proposed, based on mechanisms of homeostasis at a subcellular level. Theories of viral carcinogenesis are thought to be derived from a misinterpretation of the significance of subcellular particles. According to the author 2 types of particles are forced to multiply under artificial conditions of tissue culture or tumor transplantation. These are cytoplasmic particles deriving from mitochondria and their membranes, and are thought to be analogous to the milk agent and the Ross agent, and nuclear or Golgi particles analogous to the polyoma virus. Regulation of excessive growth is assigned to Ehrlich's mastocytes, thought to derive from large and medium sized mast cells of the thymus. It is stated that the metachromatic granules observed in unfertilized eggs and thought to be precursors of mitochondria-sized granules are the precursors of mitochondria-sized granules observed in certain mastocytes, and of the PAS-positive granules observed in the mastocytes. (13 references)

661 A UNIFYING CONCEPT OF THE GENESIS OF CANCER. (E.) Horsfall, F. L., Jr. (Sloan-Kettering Inst. Cancer Res., New York). Univ. Int. Cancr. 19(3-4):668-669, 1963.

A brief discussion of the many physical, chemical and biological factors that can produce cancerous transformation. Since the properties of cancer cells appear in new generations of cells, even when inducing factors are not present, it is likely that the alterations affect the genetic apparatus. This unifying concept serves to embrace all types of cancer cells and makes unnecessary choice among conflicting hypotheses as to the origin of cancer. (No references)

64-1662 ROLE OF THE THYMUS IN MOUSE LEUKEMIAS. (Fr.) Duplan, J. F. (Radiol. Serv., Pasteur Inst., Paris). Path. Biol. (Paris) 11(15-16/17-18):917-927, 1963.

A review is presented of both the direct and indirect effect of the thymus in spontaneous and induced leukemias in the mouse. (88 references)

64-1663 THE COMPLEX ETIOLOGY OF CANCER. (E.) Southam, C. M. (Sloan-Kettering Inst. New York). Cancer Res. 23(8):1105-1115, 1963.

The recognized causes of cancer are briefly reviewed, and the inadequacy of present knowledge to explain cancer incidence and distribution is pointed out. New knowledge and concepts concerning carcinogenesis are then discussed, emphasizing the combined effect of multiple factors; recent advances in the knowledge of the nature, growth, and pathogenicity of viruses; and the role of host factors. The concept of a complex etiology--the concurrent or sequential action of multiple etiologic factors (co-carcinogenesis in its broadest definition)--is suggested as a plausible explanation for the incidence patterns of clinical cancer. (151 references) (Author summary)

64-1664 CHROMOSOME PATTERNS IN PRIMARY NEOPLASIA. (E.) Hauschka, T. S. (Roswell Park Mem. Inst., Buffalo). Exp. Cell Res. Suppl. 9:86-98, 1963.

In a review data has been correlated on chromosome patterns in benign and malignant effusions, on modal karyotypes in solid cancers examined directly, on aneuploidy in normal and leukemic mouse marrows, and on chromosome patterns in normal and leukemic human marrows. It is proposed that phenotypic manifestations depend on the degree of balance in the karyotype as a whole, with 3 major mechanisms capable of upsetting the orderly flow of messenger RNA from a diploid set of genes: mutation in the narrow sense; large chromosomal aberrations, and infection by viral or other extrinsic DNA or RNA. Changes in the variety, amount, or timing of RNA messengers disorients protein synthesis, leading to possible isolation of the cell from growth regulation by the host. Three possible outcomes are envisioned from such isolation: metabolic deficiency, cell death, or cancer. (40 references)

PHYSICAL CARCINOGENESIS

64-1665 EXPERIMENTAL INVESTIGATIONS OF THE EFFECT OF PHOTODYNAMIC REACTIONS ON THE INDUCTION OF CANCER BY LIGHT. (Ger.)

Büschel, K.-H. M. zum (Clin. Derm., U. Hamburg, Germany) and K. Wulf. Strahlentherapie 121(3):464-473, 1963.

Groups of Wistar rats were irradiated with UV light 58 times during 170 days and were treated 58 times with Meladinin (8-methoxypsoralen) p.o. or with hematoporphyrin, i.p., resp. In the area exposed to light irregular acanthoses and hyperkeratoses developed. Tumor development did not occur up to 1½ yr. after finishing the experiments. The control animals never showed pathological skin reaction. Thus the photodynamic light reaction as a carcinogenic principle is confirmed and this correlates with clinical results.

64-1666 THE AMOUNT OF Sr⁹⁰ IN THE BONES OF PEOPLE WHO HAVE DIED OF LEUKEMIAS.

(E.) Aleksandrowicz, J. (III Clin. Int. Dis., Acad. Med., Cracow, Poland), L. Tutaj, M. Wazewska-Czyzewska and B. Marchand. Blood 22(3):346-350, 1963.

The authors have compared the amounts of Sr⁹⁰ in the bones of persons who have died of leukemias and in the bones of those deceased from causes other than tumors or hemocytopathic diseases. The first group shows an abnormally low level of Sr⁹⁰ which the authors believe to be due to disturbed calcium metabolism. (Author summary)

64-1667 LATE EFFECTS OF THOROTRAST IN CEREBRAL ANGIOGRAPHY. (E.) Blomberg, R.

(Radiophysics Inst., Karolinska Hosp., Stockholm), L.-E. Larsson, B. Lindell and E. Lindgren. Acta Radiol. (Stockholm) 1(4):995-1006, 1963.

A follow-up study of part of a total material of about 1,000 cases which received Thorotrast inj. during the yr. 1932-1947 is reported. Special attention was paid to the appearance of malignancies and the consequences of extravascular deposits of Thorotrast. About half the cases that received extravascular deposits developed severe late complications. Six cases of the total material had hepatic tumors, the incidence apparently being related to the amount of Thorotrast inj. (Author summary)

64-1668 RENAL DISEASES AND KIDNEY CANCERS IN THE RAT INDUCED BY LOCAL IRRADIATION.

(Fr.) Maldaque, P. (Cancer Inst., Louvain, Belgium). Acta Un. Int. Cancr. 19(3-4):697-703, 1963.

Renal parenchyma is much more radiosensitive than previously assumed. One single dose of

X-rays, 800 r or more, kills 100% of the animal. First cortical lesions appear in the convoluted tubules and the glomerular capillaries. If one single kidney is irradiated, the other remains functional, a very pronounced nephrosclerosis appears after a short time in the irradiated kidney, as was described previously by Zollinger. What was unknown, is that an important number of benign and malignant tumors of renal origin may occur in the atrophic kidney. The latency is long. One has the feeling that a threshold dose for renal cancerization by X-rays exists, for we never observed renal tumors in our controls, nor in animals having received 400 r on one kidney. (Author summary)

64-1669 RADIATION, GENES AND CHILDHOOD. (E.)

Mitchell, T. G., H. A. Pearson, and J. D. McIlraith. Clin. Proc. Child. Hosp. (Wash.) 19(10):263-276, 1963.

A symposium is reported which deals with many aspects of the use of radiology in medicine and the potential genetic hazards and that associated with induction of malignancies and mutations. It is stressed that all steps possible should be taken to save the child's X-ray burden for some time later in his life when he may really need it for a life-threatening situation.

64-1670 ONE CASE OF FRONTAL OSTEOMA CAUSED BY ATOMIC BOMB INJURY. (Jap.)

Yamashita, T. and S. Ueda. Hiroshima Igaku (J. Hiroshima Med. Assn.) 16(6):473-476, 1963.

A case is described of a 35-year old female with an osteoma of the right frontal sinus which was successfully treated by surgery without disturbing the appearance of the face. The most likely cause of the osteoma was considered to be trauma of the frontal area of the head suffered at the time of exposure to the atomic bomb 17 yr. previously.

64-1671 ATOMIC BOMB EXPOSURE AND ABSENTEEISM AMONG SHIPYARD WORKERS. (Jap.)

Komatsu, T. (Nagasaki Hosp., Mitsubishi Shipyard Co., Japan), G. Hashimoto, S. Ohnishi, and H. Fuzisawa. Hiroshima Igaku (J. Hiroshima Med. Assn.) 16(4):258-268, 1963.

A study was made of absenteeism and general health of male shipyard workers who were exposed to the atom bomb blast at Nagasaki compared to other workers who were not exposed at all. There was no difference in frequency of absenteeism in the exposed group classed as "far-distant" compared to the non-exposed group. There was a tendency for more frequent absences in the "near-distant" group who had had acute symptoms than

same group without acute symptoms; the latter, however, was more frequently hospitalized. The "far-distant" and non-exposed groups, absences were chiefly due to diseases of the digestive organs; in the "near-distant" exposed absences were due chiefly to diseases of the respiratory system. There were no differences in incidences of disease which could be definitely related to bomb exposure among groups exposed at various distances.

672 SERUM BUTANOL EXTRACTABLE IODINE VALUES FOR ADOLESCENTS EXPOSED IN NAGASAKI. (Jap.) Burrow, G. N. (Dept. Yale U. Sch. Med., Conn.), H. B. Hamilton, J. B. Man. Hiroshima Igaku (J. Hiroshima Assn.) 16(4):252-257, 1963.

butanol extractable iodine (BEI) values studied in a group of 249 generally healthy adolescents who were 15 years of age and were probably exposed in utero to the atom bomb in Nagasaki. There was no statistical difference in BEI values of those exposed compared to a non-exposed control group.

73 A CASE OF SPINOCELLULAR CANCER OF THE SKIN FOLLOWING ROENTGEN-RAY DERMATITIS. Hamada, T. (Dept. Derm. Urol., Osaka U. Sch. Med., Japan) and K. Murakami. No Rinsho (Clin. Derm.) 5(7):448-451,

of post-irradiation carcinoma (spinocellular) is reported; a review of pertinent literature is also presented. The pt. had received X-ray treatment for tubercular peritonsillitis.

74 NEOPLASMS IN CHILDREN TREATED WITH X-RAYS FOR THYMIC ENLARGEMENT. I. TUMORS AND MORTALITY. (E.) Pifer, J. W. (Prev. Med. Comm. Health, U. Rochester Med. Dent., N. Y.), E. T. Toyooka, R. W. Ames, W. R. Ames and L. H. Hempelmann. Cancer Inst. 31(6):1333-1356, 1963.

Graphic information and radiation factors presented for 2,809 children treated with X-rays for thymic enlargement in an upstate New York county between 1926 and 1957. Approximately half the children had been studied previously. Information regarding the health and mortality of the treated children of both sexes was collected by mail survey in 1959-60. All the children were irradiated before the age of 6 mo. Many of the older children were given relatively high doses of X-rays to areas that often involved the posterior as well as the anterior aspects of the chest. Younger children were usually given lower doses of X-rays to relatively small anterior areas. The 1,451 children previously studied

had a high incidence of tumors, particularly leukemia and thyroid neoplasms. The present survey shows that these children continued to develop tumors at a higher rate than that of their untreated siblings and higher than that expected in a comparable group from the general population. Thyroid adenomas and carcinomas comprise about one half, and osteochondromas, about one sixth of all tumors. No new cases of leukemia have occurred since the previous survey. Several cases of salivary gland tumors and neurilemmomas, which are very rare neoplasms in children and young adults, were observed. Data on mortality of treated children and their siblings in both series are difficult to evaluate. The moderate excess of deaths in the children of series I after the 1st year of life can be attributed largely to 6 cases of leukemia. Relatively few other deaths have resulted from malignant disease. (Author summary)

64-1675 NEOPLASMS IN CHILDREN TREATED WITH X-RAYS FOR THYMIC ENLARGEMENT. II. TUMOR INCIDENCE AS A FUNCTION OF RADIATION FACTORS. (E.) Toyooka, E. T. (Div. Exp. Radiol., U. Rochester Sch. Med. Dent., N. Y.), J. W. Pifer, S. L. Crump, A. M. Dutton and L. H. Hempelmann. J. Nat. Cancer Inst. 31(6):1357-1377, 1963.

The tumor incidence in 2,809 children treated with X-rays for thymic enlargement was analyzed in terms of the dose and other radiation factors. Because of the small number of specific types of neoplasms, the tumors were combined for analysis into 3 categories: 1) all thyroid tumors, 2) other tumors inside the directly treated tissues, and 3) tumors outside the directly treated tissues. A striking increase of all neoplasms, less marked for tumors outside the treated tissues, was noted as the children grew older. This complicated the analysis because the older children usually received higher doses through larger ports, frequently placed posteriorly as well as anteriorly. When the age relationship was corrected by the use of cohort analysis, a given air dose admin. half anteriorly and half posteriorly to the chest was associated with a significantly higher tumor incidence than that observed when the same total dose was given only anteriorly. Attempts to demonstrate a dose dependence for the major treatment groups, i.e., combined anterior and posterior, and anterior treatments were unsuccessful. The failure to show a dose response was attributed to the small number of neoplasms, rather than to definite evidence of an absence of such an effect. The clustering of tumors in the directly irradiated tissues and the apparent effect of port arrangement on tumor incidence constitute strong circumstantial evidence favoring radiation exposure as an etiologic factor in tumor production. The apparent effectiveness of combined anterior and posterior irradiation in inducing tumors could be due to exposure of certain tissues in the head and neck with this port arrangement.

These tissues, including the pituitary gland, were not likely to be exposed when anterior ports alone were used. Possibly the 2-wk. interval between treatments of the group of children with the highest tumor incidence also augmented the oncogenic action of the radiation exposure. (Author summary)

64-1676 REVERSAL OF THE THYMUS-DEPENDENT INFLUENCE IN RADIATION LEUKEMOGENESIS OF C57BL MICE. (E.) Law, L. W. (NCI, Bethesda), T. R. Bradley and S. Rose. J. Nat. Cancer Inst. 31(6):1461-1477, 1963.

A striking inhibition of lymphocytic neoplasms was observed in C57BL strain thymectomized and irradiated mice bearing isogenic grafts of thymic tissue under the renal capsule. A frequency of less than 5% was observed in each of 3 groups. In contrast, thymectomized and irradiated C57BL mice bearing isogenic thymic grafts in the s.c. connective tissues developed a frequency of disease, with a mean age at death approaching the pattern found in intact, fractionally irradiated mice. Grafted thymic tissue was invariably found to be lymphosarcomatous. Microscopic examination at serial intervals of thymic tissue grafted at each site showed no pronounced differences. Well-developed grafts with morphologically preserved thymic architecture persisted under the renal capsule for as long as 14 mo. Possible mechanisms for this inhibition are suggested and discussed. (Author summary)

64-1677 EXPERIMENTAL STUDIES ON THE MECHANISM OF TERATOGENIC ACTIVITY OF NOISE. THE ROLE OF THE MATERNAL ADRENALS. (Jap.) Shidara, T. (Dept. Otorhinolaryng., Fac. Med., Gunma U. Japan). Nippon Jibiinkoka Gakkai Kaiho (J. Otorhinolaryng. Soc. Jap.) 66(3): 532-547, 1963.

When pregnant Wistar rats were treated with bilateral adrenalectomy (adx.) + deoxycorticosterone acetate (0.5 mg by inj.) on day 8 of gestation, no fetal macroscopic deformities were found on sacrifice at day 19. Noise (described as white noise of 110 phon) admin. 6 hr./day to pregnant rats from day 9-15 of gestation caused no fetal malformations, but noise + a 1% soln. of trypan blue (TB; 1.0 ml/100 g body wt. s.c. on day 7 of gestation) caused many deformed fetuses and the incidence of deformities was significantly lower than in non-adx. animals. In animals subjected to bilateral adrenal medullectomy before pregnancy, TB and noise stimulation did not cause a significant difference from the control in the incidence of deformities.

64-1678 THE EFFECT OF X-RADIATION ON THE EXCRETION OF RADIOACTIVE PHOSPHORUS BY THE URINE IN RATS. (E.) Koloušek, J. (Fac. Gen. Med., Charles U., Prague) and Z. Dienstbier. Neoplasma (Bratisl.) 10(4):387-396, 1963.

Radioactive phosphorus was applied i.p. within an hour after X-irradiation of rats, and its excretion was followed at intervals of 6, 12, 24, and 72 hr. after irradiation with doses of 10, 50, 100, and 600 r. Doses of 10 and 25 r lowered the level of P³² in the urine of rats, as compared with a control group. From the dose of 50 r there occurs a significant rise in the excretion of P³². At the dose of 100 r this rise is still more accentuated. After doses of 100 and 600 r there is a one-order difference between the amount of P³² excreted by irradiated animals and that observed in control animals. Following admin. of 2,4-dinitrophenol, excretion of P³² is increased in the same way as after irradiation. The increased excretion of P³² in the urine of rats after irradiation with X-rays, as well as after the admin. of 2,4-dinitrophenol is explained as a disturbance of oxidative phosphorylation.

See also abstract nos.: 1653, 1712, 1780

CHEMICAL CARCINOGENESIS

-1679 ADENOCARCINOMA INDUCED IN THE UTERINE HORN OF MOUSE BY MEANS OF 20-MC STRING. (Jap.) Dept. Obstet. Gynec., Osaka U. Sch. Med., Japan. Rinsho Fujinka Sanka (Clin. Gynec. Obstet.) 17(3):189-190, 1963.

-Methylcholanthrene and wax (ratio 1:3), was used to infiltrate No. 12 cotton string; this was inserted and fixed in the uterine horn of the mouse. After a period of 18 wk. (no details), adenocarcinoma measuring 1.0 x 2.0 x 2.5 cm was induced in the uterine horn and metastasis to the regional lymph nodes was noted.

-1680 INDUCTION OF TUMOURS OF THE STOMACH IN RATS AND MICE BY N-NITROSO-N-ALKYL-URETHANES. (E.) Schoental, R. (Toxic. Res. Inst., Med. Res. Council Lab., Carshalton, Surrey, England). Nature (London) 199:190, 1963.

Proliferative lesions of the glandular part of the stomach were produced in rats by N-methyl-N-nitrosourethan (2.5 mg/mo. x 2, intragastric). Such squamous carcinomas sometimes accompanied foci of hyperplasia in some animals (see CRA 1(8):#1501, 1963). In 7 white male mice given N-methyl-N-nitrosourethan (4 oral doses of 1-2 mg in aqueous ethanol given over a period of 10 mo.) produced squamous carcinomas in 4/7 (44%) presenting in addition a sarcoma), and among 11-13 mo. survivors a papillary growth with no evidence of invasiveness in 1/7. It is suggested that small variations in the site of deposition of the agents from the stomach may be responsible for variations in tumor location and type. (See also CRA 1(3):#449, 1963.)

-1681 THE INFLUENCE OF THE CARCINOGEN N-NITROSO-N-AMINOAZOTOLUENE ON THE REACTIVITY OF LIVER CELLS AFTER PARTIAL HEPATECTOMY. (E.) Kuans-Hua (Inst. Exp. Clin. Oncol., Acad. Sci. USSR, Moscow). Biull. Eksp. Biol. Med. 53(5):592-594, 1963.

Domestic bred mice were painted 3 times with 1% N-nitroso-N-aminoazotoluene (OAAT; in benzene) at 2-day intervals. On the fourth day after the last painting, partial hepatectomy was performed. The mice were killed 30, 36, 48, 54, 60, 72 and 78 hr. after operation. OAAT inhibited the mitotic activity of liver cells in the hepatectomized mice, but no inhibition was observed in the control mice painted with benzene, or with the carcinogen diethylaminoazobenzene. (Author summary)

-1682 STUDIES OF MOUSE LIVER PROTEIN BIOSYNTHESIS IN o-AMINOAZOTOLUENE INDUCED MALIGNIZATION. (Rus.) Drozdova, G. A. (Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR,

Moscow) and S. Ia. Davydova. Vop. Med. Khim. 9(5):469-475, 1963.

Some increase in amino acid synthesis was observed in mouse liver within 3 mo. after admin. of o-aminoazotoluene (OAAT). The amino acid synthesis tends to decrease gradually in the course of the experiment. In induced hepatoma, decrease in amino acid activation rate was more distinct. Velocity of labeled amino acid incorporation in S-RNA was increased within 3 mo. after OAAT admin. During the second period (3-8 mo.) after beginning of the experiment, protein biosynthesis rate was decreased two-fold as compared with controls. In induced hepatoma no difference in protein biosynthesis rate as compared with normal liver could be observed. Alterations in protein biosynthesis rates in cancerogenesis reflect the nature of the morphological damage to liver tissue. (Author summary)

64-1683 INDUCTION OF SARCOMA IN RATS BY SUBCUTANEOUS INJECTION OF 4-HYDROXYLAMINO-QUINOLINE N-OXIDE. (E.) Endo, H. (Div. Chem., Inst. Cancer Res., Kyushu U., Fukuoka, Japan) and F. Kume. Naturwissenschaften 50(15):525-526, 1963.

Injection s.c. of 4-hydroxylaminoquinoline N-oxide-HCl (HAQO; 1% in peanut oil:cholesterol (100:5), 0.1 ml x 10 over 100 days) to female rats (Oosama strain) caused fibrosarcomas at the inj. site in 3/20 animals inj. repeatedly in the right groin, but in only 1 in 20 inj. s.c. in the abdominal wall (this 1 rat was inj. once in the groin). No tumors developed in controls given only the vehicle. The tumors were palpable at 130 days and the animals were autopsied at 137 days. It is mentioned that in preliminary experiments painting the back with HAQO-HCl in alcohol failed to induce tumors. The results indicate that the nitro group of the quinoline group of 4-nitroquinoline N-oxide is not indispensable for carcinogenic action, and it is suggested that the biological effect of the latter compound might be through the reduced form.

64-1684 EXPERIMENTAL PULMONARY ADENOMA DUE TO URETHAN IN THE SWISS MOUSE. II. ELECTRON MICROSCOPE CYTOLOGICAL STUDY. (Fr.) Driessens, J. (Cancer Res. Inst., Lille, France), A. Dupont and A. Demaille. C.R. Soc. Biol. (Paris) 157(3):560-563, 1963.

Electron microscope studies are presented of the previously reported pulmonary adenomas induced by urethan in Swiss mice (see CRA 1(2):#233, 1963) and which were observed for 20 wk. The tumors consisted of dark and light cells in variable proportions, forming initially a compact adenoma and evolving by the 15th-17th week

into papillary adenomas, both forms being concurrent at times. Changes in the ultrastructures of the nucleus and nucleolus, the cellular membrane, the mitochondria and the ergastoplasmic-mitochondrial complex are described. In the established adenoma, the tumor cell resembled a normal liver cell (clearly delimited cell of the same size with a round nucleus and dense cytoplasm including a few opaque mitochondria). By the 20th week in such a cell the mitochondria could either be round with ribbon-like internal cristae and osmiophilic granular inclusions, or elongated with a double external membrane and short parallel internal cristae. Examination of the transition zone between the adenomatous foci and the normal parenchyma indicated that the adenomatous changes originated in the alveolar wall and not in the bronchiolar lining, although the evidence on this point was not conclusive.

64-1685 EXPERIMENTAL PULMONARY ADENOMA DUE TO URETHAN IN THE SWISS MOUSE. HISTOLOGICAL STUDY. (Fr.) Driessens, J. (Cancer Res. Inst., Lille, France), A. Clay, J. Vanlerenberghe, A. Dupont, A. Demaille and L. Adenis. Bull. Assn. Franc. Cancer 50(2):171-182, 1963.

Additional data supplements two previously published reports (see CRA 1(2):#233, 1963 and *ibid.*, CRA 1(9-10):#1684, 1964). When the observations were carried beyond the 20th wk. to the 39th wk., histological examinations revealed the transformation of the papillary adenomas into atypical epitheliomas, a true picture of alveolar carcinomatosis being the end result. Metastases were not seen. Cytologically too the transformation to malignancy was obvious from the 25th week on with widespread anaplastic dedifferentiation. Neoplastic emboli were occasionally formed in the blood vessels. No trace of a virus was found at any stage.

64-1686 CARCINOGENIC ACTION OF N-HYDROXY-4-ACETYLAMINOSTILBENE. (E.) Baldwin, R. W. (Cancer Res. Lab., U. Nottingham, England), W. R. D. Smith and S. J. Surtees. Nature (London) 199:613-614, 1963.

Rats on a low protein diet were fed 4-dimethylaminostilbene (DMAS), 4-acetylaminostilbene (AAS), or N-hydroxy-4-acetylaminostilbene (HAAS), approx. 0.5 mg/day in the diet for 22-32 wk. The last compound was highly toxic to females with only 6/16 surviving at 22 wk. The percentage of ear duct carcinomas (all squamous in type), detected between 20-60 wk. in males and females, resp., was: DMAS 55 and 55, AAS 88 and 85, and HAAS 86 and 83. In rats fed the HAAS, 1 abdominal fibrosarcoma and 1 intestinal adenocarcinoma were also observed.

64-1687 OVARIAN TERATOMA IN THE MOUSE. (E.) Thiery, M. (Gynec. Sect., Ghent State U., Belgium). Brit. J. Cancer 17(2):231-234, 1963.

Two primary, solid, histologically benign teratomas of the ovary occurred in two adult members of a colony of C3H/N mice. The first mouse was pregnant, the second had been treated with 3,4-benzopyrene and estriol. This report describes the histopathological features of these very rare tumors. It draws attention to the possible teratogenous action on the ovary of the hydrocarbon used. (Author summary)

64-1688 EVALUATION OF CARCINOGENIC ACTIVITY OF FOOD ADDITIVES AND CONTAMINANTS. (E.) Truhaut, R. (Dept. Toxicol., U. Paris, France). Arch. Environ. Health (Chicago) 7(3):351-358, 1963.

A discussion is presented of methodology that should be employed in the evaluation of the potential carcinogenicity of food additives and contaminants as well as the reasonable evaluation of results. See also CRA 1(1):#33, 1963.

64-1689 3,4-BENZOPYRENE CONTENT IN SMOKED SPRATS PREPARED FROM SMOKE FROM THE FRICTION SMOKE GENERATOR AND PSM VNIRO GENERATOR. (Rus.) Gorelova, N. D. (Inst. Oncol., Acad. Med. Sci. USSR, Moscow), P. P. Dikun, O. P. Gretskaia and A. V. Emshanova. Vop. Onkol. 9(8):77-80, 1963.

When tested, only 1/5 smoke samples from the American friction smoke generator contained a detectable amount of 3,4-benzopyrene (BP). In sprat and sausage smoked in this generator at 30-40°C for 10 hr. the amount of BP was 0.2 µg/kg and 0.12 µg/kg, resp. No BP was found in cold or hot smoke from the PSM VNIRO generator, yet in 0.07 and 0.18 g tar obtained from the smoke the amount of BP was 3 and 6 µg, resp. BP content of sprats and herrings smoked in this generator was 0.27-7 µg/kg and 0.4-0.7 µg/kg, resp. In fish processed in hot smoke in this generator the amount of BP was much less when sawdust was burned than when wood was burned. When the latter was used, av. BP content of fish was 3 µg/kg.

64-1690 LEUKEMIA-PRODUCING ACTION OF NUCLEIC ACIDS ISOLATED FROM TUMORS. (E.) Bressler, V. M. (Inst. Cytol., USSR Acad. Sci., Leningrad U.), R. G. Broun, D. Ya. Podgaetskaya and I. N. Shvemberger. Fed. Proc. 22(3):T571-T575, 1963.

The admin. of preparations of RNA containing an admixture of DNA, isolated from tumors, to adult C57BL and newborn mongrel mice caused the rapid development of myeloid leukemia in a high proportion of animals. The most active preparation was isolated from Ehrlich's carcinoma; the preparations obtained from human leukemic tissues were less active. Besides the usual forms, tumor-like forms of myeloid leukemia were sometimes induced by nucleic acids. The leukemia-producing activity of deproteinized preparation

nucleic acids cannot be explained by the transfer of a virus. It is admitted that virus nucleic acid may enter the cells, that the nucleic acid of the tumor donor cells, administered outside, may be included into the genetic apparatus of the recipient cells, and that the action of the nucleic acids which were injected may be a factor causing inherited mutations in the recipient cells. These 3 explanations must be regarded as equally probable at the present time. (Author summary)

1691 TOXIC EFFECTS OF STEROID HORMONES ON ORGAN CULTURES OF MOUSE MAMMARY TUMORS, WITH A COMMENT ON THE OCCURRENCE OF VIRAL INCLUSION BODIES. (E.) Rivera, E. M. (U. Reading, England), J. J. Elias, H. A. Bern, N. P. Napalkov, and D. R. Pitelka. *J. Nat. Cancer Inst.* 31(3): 1-687, 1963.

Primary adenocarcinomas from C3H/CrGl mice were cultured for 5 days in medium 199 supplemented with the following steroids in conc. ranging from 0.02 to 200 µg per ml: estrone, estradiol, progesterone, cortisol, corticosterone, and deoxycorticosterone. All steroids were toxic at the higher dose levels. Occurrence of cytoplasmic inclusions, representing accumulations of virus-like particles, was also noted as a result of organ culture of these tumors, with and without hormone supplementation of the medium. No consistent effect of the steroids on the occurrence of inclusions, or on the histology of the transplanted tumors, was noted.

1692 ON AN EXPLANATION OF AUTORADIOGRAMS WITH LABELED AMINO ACIDS BY A GENERALLY VALID SCHEME OF CELLULAR INCORPORATION, THE EFFECT OF BUTTER YELLOW (DAB) CARCINOGENESIS. (Ger.) Maurer, W. (Inst. Med. Isotopes, U. Cologne, Germany), K. J. Lennartz and Hempel. Pp. 512-524 in *Radioaktive Isotope in Klinik und Forschung*. 5. Band. (Radioactive Isotopes in the Clinic and Research. Vol. 5.) Reports of the International Symposium in Stein, 1962. Fellingner, K. and R. Höfer (eds.). Urban and Schwarzenberg, Munich and Berlin, 566 pp., 1963.

Following the admin. of tritiated amino acids to mice and other animals, the animals were sacrificed 1 hr. later and the incorporation of nuclei and cytoplasm of cells from different organs was determined by autoradiography and grain counting. A comparison of different cell types showed that nuclear incorporation was proportional, more or less, to the nuclear volume. For all cell types cytoplasmic labeling was 5-10x greater than nuclear labeling. According to the relative volume of the cytoplasm (cytoplasm-nucleus-volume-relationship) cytoplasmic incorporation per unit of volume varies considerably from cell type to cell type.

These relationships were also studied during cancerization of the rat liver following Butter Yellow. Marked differences in cytoplasmic and nuclear label incorporation between normal, and hepatoma, and carcinoma cells could be demonstrated. All results were very similar for different tritiated amino acids tested. Apparently the autoradiographs reflect the protein metabolism of the various cell types. The influence of self-absorption of the tritium β-particles in the material of the histological sections was studied. (Author summary)

64-1693 A METHOD FOR DETERMINING CILIASTATIC COMPONENTS IN CIGARETTE SMOKE. (E.) Wynder, E. L. (Sloan-Kettering Inst. Cancer Res., New York), H. E. Kaiser, D. A. Goodman and D. Hoffmann. *Cancer* 16(9):1222-1225, 1963.

A simple method has been described, utilizing the gill lamellae of the fresh-water mussel (*Lamellibranchiata unio*), to study ciliastasis-inducing components. Smoke from a single puff (35 ml) of an 85-mm nonfilter cigarette produced immediate stasis of gill cilia. The ciliastatic effect of water extracts of cigarette smoke condensate fractions was, in decreasing order: acidic, weak acidic, insoluble, basic, and neutral. Phenols, as present in cigarette smoke, stopped ciliary movement more rapidly and in lower conc. than did nicotine in mussel gill. The effect of cigarette smoke on mussel gill cilia appears to be due, at least in part, to specific constituents in the smoke. (Author summary)

64-1694 COMPARISON OF THE YIELDS OF SEVERAL SELECTED COMPONENTS IN THE SMOKE FROM DIFFERENT TOBACCO PRODUCTS. (E.) Hoffmann, D. (Sloan-Kettering Inst. Cancer Res., New York), G. Rathkamp and E. L. Wynder. *J. Nat. Cancer Inst.* 31(3):627-637, 1963.

Smoke of a plain 85 mm cigarette, 2 types of cigars, a pipe with standard pipe tobacco, a pipe filled with cigarette tobacco, and a Syrian water pipe was analyzed for the mainstream particulate matter, nicotine, benzo[a]pyrene (BP), and phenols. On the basis of equal weights of tobacco consumed, cigarettes gave the highest yields of both nicotine and particulate materials, with lesser amounts, in decreasing order, obtained from an American-type pipe, cigars, and an oriental water pipe. The highest value from 100 g tobacco for BP, 27.0 µg, and phenol, 68.7 mg, was found in the smoke of a pipe filled with standard pipe tobacco. A pipe filled with cigarette tobacco yielded BP, 10.5 µg, phenol, 21.2 mg; cigarette smoke, BP, 7.8 µg, phenol, 25.4 mg; cigar smoke, BP, 4.0 and 5.1 µg, phenol, 7.4 and 10.7 mg, with the lowest values for the smoke from an oriental water pipe, BP, 1.7 µg, phenol, 1.8 mg. The water-filled oriental pipe retained about 90% of the phenol

of the original smoke. Particulate matter, nicotine, and BP were retained to a lesser degree by the water (about 50%). Increased puff frequency resulted in higher yields of all 4 groups of compounds in the mainstream smoke. Values at 2 puffs per minute frequency ranged from 50-120% higher than those at 1 puff per minute when the other smoking factors were held constant. Since biological tests and comparisons of the carcinogenicity of the condensates of cigarettes, cigars, and pipes have previously been carried out on equal weights of condensate, the analytical results of this study were compared in the same manner. One g of the smoke condensates from 85 mm plain cigarettes, 2 types of cigars, and a standard pipe contain 1.25, 3.6, 3.9, and 6.0 μ g BP, resp. The corresponding phenol values were 4.1, 6.7, 8.2, and 15.0 mg per 1 g smoke condensate. (Author summary)

- 64-1695 CARCINOMA OF THE GLANDULAR STOMACH INDUCED IN FEMALE C57L MICE BY INTRAPARIETAL INJECTION OF 20-METHYLCHOLANTHRENE. (Sp.) Vilches, C. A. and J. M. Echave Llanos. Rev. Argent. Cancerol. 4(2):109-114, 1962.

An experiment was performed to study the production of neoplasms of the glandular stomach in female C57L mice by intraparietal inj. of 20-methylcholanthrene (0.3 mg in 0.01 ml of an aqueous suspension of gum arabic). Of 18 animals, 13 presented neoplasias, with 6 invading the submucosa, 5 the peritoneum and 2 the liver; 3 animals presented intramucosal hyperplasias. Five animals had lesions in the fundus, 3 in the antrum, 1 in the pylorus, 3 in the fundus and antrum simultaneously and 1 in the fundus and pylorus. See also CRA 1(4): #651, 1963.

- 64-1696 CARCINOGENIC SUBSTANCES IN WATER AND EARTH. XIV. FURTHER INVESTIGATIONS ON POLYCYCLIC AROMATIC HYDROCARBONS IN EARTH SAMPLES. (Ger.) Borneff, J. (Inst. Hygiene, Johannes Gutenberg-U., Mainz, Germany) and H. Kunte. Arch. Hyg. Bakt. 147(6):401-409, 1963.

Soil samples which were taken in spruce and beech woods, as well as in mixed woodland in the region near Lake Constance, contained (as did sand samples of Lüneburg Heath) polycyclic aromatic hydrocarbons. 3,4-Benzpyrene, 3,4-benzofluoranthene, 10,11-benzofluoranthene, 1,2-benzanthracene, chrysene and indeno(1,2,3-cd)-pyrene were detected, as well as some non-carcinogenic substances. As to quantity, a conc. of about 0.3 mg/kg was found. (Author summary)

- 64-1697 ULTRASTRUCTURE OF A MOUSE ASCITIC SARCOMA PRODUCED BY ISONICOTINIC ACID HYDRAZIDE (INH). (Ger.) Kendrey, G. (Inst. Pat. Karl-Marx-U., Leipzig, Germany) and L. Cossel. Beitr. Path. Anat. 128(2):219-237, 1963.

Electron microscopic examinations of cells of a ascites sarcoma of the mouse induced by isonicotinic acid hydrazide (INH) are described and discussed. The results correspond in detail with those found so far in ascites tumor cells and other tumor cells. As the most important finding, "virus-like particles" were seen in the nucleus and cytoplasm of tumor cells. (Author summary)

- 64-1698 LUNG CANCEROGENESIS BY ISONICOTINIC ACID HYDRAZIDE IN MALE BALB/c MICE WITH AND WITHOUT MTV. (It.) Ribacchi, R. (Div. Cancer Res., U. Perugia, Italy), C. Biancifiori, U. Milia, F. P. Di Leo and E. Bucciarelli. Lav. Ist. Anat. U. Perugia 23(2):103-114, 1963.

Lung cancerogenesis by isonicotinic acid hydrazide has been studied in BALB/c and BALB/cf substrains. No differences in the number or distribution of tumors, were found between the two strains with and without MTV. At autopsy, all the treated animals showed multiple pulmonary tumors (av. 3.1/mouse). Histologically, solid and papillary adenomas were found in all the experimental animals whereas lung carcinomas were observed in only 19 mice (45.3%). The incidence of lung carcinomas increased with the age of the animals: 9.1, 50 and 85.7%, resp. at the av. age of 12.5, 17.5 and 22.5 mo. Seven or 36.8% of mice with lung carcinomas had metastatic spread at the av. age of 586 days. (Author summary)

- 64-1699 LUNG CANCEROGENESIS BY HYDRAZINE SULFATE IN FEMALE BALB/c MICE. (It.) Biancifiori, C. (Div. Cancer Res., U. Perugia, Italy), R. Ribacchi, E. Bucciarelli, F. P. Di Leo and U. Milia. Lav. Ist. Anat. U. Perugia 23(2):115-128, 1963.

Hydrazine sulfate (1.13 mg/day, by special intragastric tube) was admin. to 84 female virgin mice; groups of 3 were killed every 10 days up to 310 days when 19 survived. The percentage of lung tumors, after the 200th day approached 100%. The induction time was about 150 days. The lung tumors were often multiple and the av. number per mouse progressively increased and rose considerably even after the interruption of treatment. At histological examination, adenomata (solid and tubular-papillary), anaplastic adenomata and carcinoma were observed. More anaplastic adenomata and carcinoma were observed in the mice which survived longer.

4-1700 COD LIVER OIL AND LYMPHOCYTOMA IN THE CHICKEN. (E., Thesis, U. Microfilms, Ann Arbor, Mich., No. 63-5743.) Fredrickson, N. (U. Wisconsin, Madison, 1963.) Dissertation Abstr. 24(1):255, 1963.

The effect of feeding one specific lot of cod liver oil on the incidence of lymphocytoma was tested. Four groups of about 100 female chickens of the susceptible line 151 were exposed at one day of age to two different sources of virus causing lymphocytoma. Two groups were placed in direct contact with equal numbers of line 151 males, inoc. with the RPL 12 strain of leukosis virus at one day of age, and 2 with an equal number of one-day-old naturally infected females of a White Leghorn-Rhode Island Red cross. One group of the line 151 females in each type of contact was fed a basal diet and the other the basal diet to which 3% cod liver oil had been added. All birds dying during the experimental period of 500 days and all survivors were examined for neoplasia. A total of 71 line 151 males died with lymphocytoma. Both groups receiving dietary cod liver oil had a higher incidence (35%) than those fed the basal diet (20%). There was no difference in the time of death from lymphocytoma or in the number of tumors induced. Most of the line 151 males died with erythroblastosis. The feeding of cod liver oil had no effect on the incidence of erythroblastosis. There was a slightly higher incidence of lymphocytoma and other tumors among the crossbred females fed cod liver oil than among those fed the basal diet alone.

4-1701 INHIBITION OF URETHAN LUNG TUMOR INDUCTION IN MICE BY TOTAL-BODY X-RADIATION. (E.) Foley, W. A. (U. S. Naval Radiol. Defense Lab., San Francisco, Cal.) and L. J. Cole. Cancer Res. 23(8):1176-1180, 1963.

A more detailed account of the paper abstracted as CRA 1(5):#817, 1963.

4-1702 RELATIONSHIP BETWEEN CHEMICALLY-INDUCED LEUKEMIA AND VIRUS PARTICLES. (E.) Irino, S. (Dept. Int. Med., Okayama Hosp., Japan). Nisshin Igaku (Jap. J. Med. Progress) 50(2):74-84, 1963.

Leukemias induced by 20-methylcholanthrene (MC) in RF mice have been found to originate first in the thymus in thymic type lymphocytic leukemia, in the spleen or lymph nodes in the non-thymic type lymphocytic leukemia, and in the bone marrow in myelogenous leukemia. It has been shown that hypoplasia of the hematopoietic organs precedes the development of leukemia. MC-induced leukemia has been successfully transmitted by cell-free material. With the aid of the electron microscope, virus particles have been demonstrated in leukemic tissue. From these facts, it is concluded that the

chemical carcinogen acts to induce leukemia by activating a latent virus naturally resident in the RF mouse. See also 1(8):#1467, 1963.

64-1703 HISTOLOGICAL PICTURE AND HORMONE DEPENDENCE OF MAMMARY CARCINOMA INDUCED BY 20-METHYLCHOLANTHRENE. (Jap.) Ishikawa, H. (Dept. Surg., Gunma Coll. Med. Hosp., Japan). Kitakanto Igaku (Kitakanto Med. J.) 13(2):115-125, 1963.

Following the intragastric admin. of 20-methylcholanthrene, 34 tumors developed in the mammary glands of 19 out of 29 female Wistar rats. Histologically the tumors were tubular adenocarcinomas of 3 types. The large duct type with cancer cells in many thick layers was seen in 8 rats; the small duct type with cells in one or two thin layers was seen in 7. Four rats showed both types. The distinctive features of the large duct type appeared somewhat late in development and growth was constant. The sex chromatin count was relatively high and was considered to be estrogen-dependent. The characteristic features of the small duct type developed at an early stage and showed rapid growth and ulcer formation. Sex chromatin count was low and was considered to be progesterone-dependent.

64-1704 NEOPLASTIC NATURE OF LIVER "BLOOD CYSTS" INDUCED BY URETHAN IN MICE. (E.) Trainin, N. (Dept. Exp. Biol., Weizmann Inst. Sci., Rehovoth, Israel). J. Nat. Cancer Inst. 31(6):1489-1499, 1963.

A more detailed account of the paper abstracted as CRA 1(6):#1064, 1963.

64-1705 ONCOGENIC DEOXYRIBONUCLEOPROTEIN AND DEOXYRIBONUCLEIC ACID ISOLATED FROM ASCITES TUMOUR CELLS. (E.) Hidvégi, E. J. ("Frederic Joliot-Curie" Natl. Res. Inst. Radiobiol., Budapest), P. Lonai, F. Antoni, E. Unger and V. Várterész. Neoplasma (Bratisl.) 10(4):361-364, 1963.

DNA and deoxyribonucleoprotein isolated from Lettre-Ehrlich ascites tumor cells, when inj. into Swiss mice, induced leukemia in 5/15 (33%) and 6/28 (21%), resp., compared to an incidence of 4/114 (3.5%) in controls.

64-1706 CARCINOMA OF THE ESOPHAGUS DEVELOPING AFTER BURNS CAUSED BY SODIUM HYDROXIDE. (Rus.) Sapozhnikova, M. A. (Dept. Path. Anat., Sklifosovski Inst., Moscow). Vop. Onkol. 9(11):91-95, 1963.

Three cases of cancer are described which developed in scars in the constricted esophagus which were caused by caustic soda burns.

Carcinoma appeared in pts. aged 22, 28 and 38, resp., in 14-20 yr. after the occurrence of burns. For many years they had been treated by insertions of bougies. Postmortem examination revealed cancer in the esophagus which was changed by the scars. In 2 cases tracheoesophageal fistulas were found.

64-1707 HORMONES IN THE GENESIS OF CANCER. (E.) Mühlbock, O. (Netherlands Cancer Inst., Amsterdam). Neoplasma (Bratisl.) 10(4):337-342, 1963.

A survey of the present state of knowledge of hormonal carcinogenesis is given. The possible mechanism of the carcinogenic effect of some hormones is discussed. The effect of estrogens on the occurrence of mammary tumors was examined in various mouse strains, with and without mammary tumor agent. The effects of dose of estrogen and the length of the period of treatment were also determined.

64-1708 ELECTRON-DONOR OR ELECTRON-ACCEPTOR PROPERTIES AND CARCINOGENIC ACTIVITY OF ORGANIC MOLECULES. (E.) Pullman, B. (Biol. Physico-chemical Inst., U. Paris, France) and A. Pullman. Nature (London) 199:467-471, 1963.

The authors attack the theory of Allison and Nash (see CRA 1(2):#204, 1963), that carcinogenicity of chemical compounds arises as a result of a suitable combination in one compound of both electron-donating and electron-accepting properties. Presented are absolute values of the energy coefficients of the highest filled (or lowest empty) molecular orbital for an entire series of polybenzenoid aromatic hydrocarbons, indicating no correlation between the electron donating and accepting properties and carcinogenicity. Examples of many molecules presenting ideal conditions for carcinogenicity according to the Allison and Nash hypothesis, but no actual biological carcinogenicity are described. Thus the authors favor a theory of carcinogenesis similar to that of mutagenesis involving a variety of different types of reactions with varied sites of nucleic acids. For aromatic hydrocarbons the authors propose a reactivity arising from characteristics and reactivities at the K and L regions (see CRA 1(3):#421, 1963). In an accompanying answer to the attack A. C. Allison and T. Nash reply that the measurements of energy coefficients presented by the Pullmans are estimates, as opposed to actual measurement of charge-transfer formation. The original theory had been presented with several modifying clauses, including the importance of steric factors, of appropriate electron distribution, and of metabolic stability. The analogy of carcinogenesis to mutagenesis is thought appropriate. However, it is pointed out that of two basic mechanisms, chemical modification of molecules

through alkylation or deamination, and intercalation of mutagen between base pairs thus altering base pair sequence, the latter mechanism almost certainly involves charge transfer and would fit the Allison-Nash model.

64-1709 A SIMPLE METHOD FOR PREDICTING THE CARCINOGENIC PROPERTIES OF LARGE AROMATIC MOLECULES. (E., Abstract) Flurry, R. L., Jr. (Dept. Chem., Louisiana State U., New Orleans). P. 23-0 in Abstracts of Papers, 145th Meet. Am. Chem. Soc. New York, N. Y. Anderson, S. (Ed.), 1963.

There have been numerous attempts to correlate the carcinogenic activity of large aromatic compounds with some theoretically predictable quantity. Most of these attempts have been relatively successful; however, the methods employed have generally been complicated enough to prevent workers who have not had a fair amount of experience in molecular orbital (MO) theory from applying them to new compounds. The purpose of this work is to point out that one of the simplest MO approximations, Dewar's approximation for localization energies, can be applied to predict, with excellent agreement, the carcinogenic properties of large aromatic systems. It is found in applying the method that compound having an active mesophenanthrenic bond (K region) with an ortho localization energy of less than 2.00β should be carcinogenic unless they have active mesoanthracenic positions (L region) with a para localization energy of less than approximately 2.9β . (Author summary)

64-1710 AN EXPERIMENTAL EVALUATION OF THE ROLE OF REGIONAL CHRONIC LYMPHOEDEMA IN NEOVASCULAR GROWTH. (E.) Tedeschi, L. G. (Framingham Union Hosp., Mass.), W. S. George, G. C. Botta and C. G. Tedeschi. S. Afr. J. Lab. Clin. Med. 9(2):41-57, 1963.

Introduction of a 3% soln. of sodium tetradecyl sulfate (STS), a known sclerosing agent + 20-methylcholanthrene (20-Me) in peanut oil, into the femoral artery of rabbits produced a disorderly proliferation of neovascular tissue. Lesions (not believed to duplicate those of Kaposi's sarcoma) occurred 3 times as frequently in animals with chronic edema (60%) as in animals without edema (20%). Similar results were obtained after inj. of 20-Me alone except that the less frequent occurrence of edema (25%) was paralleled by a less frequent development of growths, the latter occurring in 80% of the animals with regional edema and 13.3% of those without edema. In contrast to the predominantly neovascular response in the animals receiving STS + 20-Me, 20-Me alone induced a mesenchymal type of response apparently originating from mobilization of fibroblastic elements.

4-1711 EXPERIMENTAL PRODUCTION OF ABORTIONS AND FETAL MALFORMATIONS. (PRELIMINARY REPORT) (Sp.) Bedoya, J. M. (Dept. Gynec., Univ. of Seville, Spain) and J. Navarro. Rev. Esp. Obstet. Ginec. 22(129):191-194, 1963.

In guinea pigs triethylenemelamine (TEM; 0.10 g/kg/day) admin. from day 3-7 of gestation resulted in death with retention of the embryos in 2/3, and a normal + a dead fetus in 1/3. Administration of TEM on days 8-12 gave normal fetuses in 1/2, and a normal + a malformed fetus in 1/2. In contrast, tolbutamide (33 g/kg/day x 2-6 from days 4-12) to guinea pigs and rats caused death and resorption of embryos when admin. early in gestation, and occasional nophthalmia in rats when admin. late in pregnancy.

4-1712 EFFECTS OF WHOLE BODY IRRADIATION AND OF PARTIAL HEPATECTOMY ON THE LIVER LESIONS INDUCED IN RATS BY A SINGLE DOSE OF RETRORSINE, A PYRROLIZIDINE (SENECIOALKALOID). (E.) Schoental, R. (Toxic. Res. Unit, Med. Res. Council Lab., Carshalton, Surrey, England) and J. P. M. Bensted. Brit. J. Cancer 7(2):242-251, 1963.

Rats which survived 100 days after a single oral dose of retrorsine (R; 30 mg/kg) were exposed to whole body X-irradiation (400 r); 5 of these rats survived more than a yr. after the alkaloid and developed a variety of tumors at various sites. Primary liver tumors, one of which was a hepatocarcinoma with metastases in the lung, were present in 6 rats. Among 9 rats which survived more than a yr. after a single oral dose of R (30 mg/kg) and received no further treatment, 5 developed hepatoma. Two hepatomas were present among 9 rats which were given a single oral dose of R (30 mg/kg) following partial hepatectomy. Tumors at various sites (but not of the liver) were present in 6 rats which survived more than one yr. after whole body irradiation (400 r). Whole body irradiation or partial hepatectomy did not inhibit the development of chronic liver lesions and liver tumors caused by a single oral dose of R. On the basis of the present experiments there is no definite evidence of a synergistic action due to these agents. (Author summary)

4-1713 EFFECT OF THYMECTOMY ON THE INDUCTION OF SKIN TUMOURS BY 3,4-BENZOPYRENE. (E.) Miller, J. F. A. P. (Chester Beatty Res. Inst., Royal Cancer Hosp., London, S.W.3), J. A. Grant and F. J. C. Roe. Nature (London) 199:920-922, 1963.

Mice of a colony bred albino stock (originally from S. Schofield of Oldham) were thymectomized at 3 days and painted from 5 wk. of age with 3,4-benzpyrene (50 µg in 0.2 ml acetone 2x/wk. for 20 wk.). By 100 days after the start of

treatment papillomas were present in 7/16 thymectomized and in 1/22 sham-operated controls, although the final incidence after 170 days was similar, 16/16 and 21/22, resp. In thymectomized mice, however, 10% (14/134) of the papillomas regressed, and 12% (16/134) progressed to carcinoma, whereas in controls 17% (33/189) regressed, and only 4% (8/189) progressed to carcinoma. Histograms indicated that papillomas grow to a larger size in thymectomized mice than in controls. Of 12 thymectomized and 12 sham-operated acetone-treated controls, 1 and 0, resp., developed papillomas. The 3-day thymectomized mice used in these experiments have reduced capacity for homograft rejection when antigenic differences between donor and host are slight.

64-1714 DEPRESSED INCORPORATION OF THYMIDINE-H³ INTO DEOXYRIBONUCLEIC ACID FOLLOWING ADMINISTRATION OF 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Jensen, E. V. (Ben May Lab. Cancer Res., U. Chicago, Ill.), E. Ford and C. Huggins. Proc. Nat. Acad. Sci. USA 50(3):454-459, 1963.

In adult or infant Sprague-Dawley rats admin. 9,10-dimethyl-1,2-benzanthracene (DMBA; i.v. in lipid emulsion, 2 mg to infants, 5 mg to adults) 4 hr. before i.v. admin. of tritiated thymidine (TdRH³) depressed the nonvolatile radioactivity in testis and adrenals of adults to 33% of that of controls, and the total radioactivity in testis (mainly acid insoluble) and ileum of infants to 32 and 11% of controls, resp. Administration of DMBA 4 hr. after TdRH³ had only slight inhibitory effects. On radioautography of DMBA-treated testis (4 hr. prior to TdRH³ inj.) there was a 50% decrease in the amount of radioactivity in testis tubules and in spermatogonia. In DMBA-treated animals a significant increase was observed in the amount of nonvolatile radioactivity in blood and tissues, sometimes exceeding greatly the nonvolatile radioactivity incorporated. In time course studies a 1 hr. lag period was observed, prior to onset of the DMBA depressive effect of TdRH³ incorporation of the testis. Subsequently depression increased linearly to 4 days, and effects were observed for up to 7 days. In other studies a log-dose relationship was observed for inhibition of TdRH³ incorporation into ileum with a range up to 5 mg DMBA, whereas for incorporation into testis max. depression was obtained after 2 mg DMBA. It is concluded that in addition to inhibition of thymidine incorporation into acid insoluble material, DMBA also stimulates metabolic degradation of the nucleoside with liberation of tritium.

64-1715 CARCINOGENIC ACTIVITY OF AROMATIC POLYCYCLIC HYDROCARBONS WITH A FLUOR-ANTHENE NUCLEUS. (Fr.) Lacassagne, A. (Radium Inst., U. Paris, France), N. P. Buu-Hoi, F. Zajdela, D. Lavit-Lamy and O. Chalvet. Acta Un. Int. Cancr. 19(3-4):490-496, 1963.

It is shown that a number of aromatic hydrocarbons belonging to the fluoranthene group possess a pronounced carcinogenic activity in mice on s.c. inj.; this is true for 3,4-benzofluoranthene, 11,12-benzofluoranthene, and 2,3-phenyleneprene. Some of these hydrocarbons exist in coal tar and tobacco tar. The electronic characteristics of these molecules have been computed by the three methods of theoretical chemistry which are currently employed, and these have not shown any correlation between the theoretical calculations and experimental results in this family of molecules which are devoid of a K-region. (Author summary)

64-1716 LIVER FUNCTION DURING AZO DYE HEPATOCARCINOGENESIS. (E.) Watters, C. (Montreal Cancer Inst., Canada) and A. Cantero. P. 32C in Abstracts of Papers. 145th Meet. Am. Chem. Soc. New York, N. Y. Anderson, S. (Ed.), 1963.

Rose Bengal excretion was used in a study of liver function during hepatocarcinogenesis. Two groups of Wistar rats were fed: one a protein deficient basal diet, the other, a similar diet to which azo dye was added at a level of 0.06%. Rose Bengal liver function test was performed in both groups, at different intervals of the feeding of the diet. Radioactive Rose Bengal 131 was inj. under Nembutal anesthesia. Bile and blood samples were collected during a period of 3 hr. after inj. The kinetics of uptake and excretion were compared for the two groups of rats. A sharp decrease in uptake was seen, on the second day, in the azo dye fed group. No such decrease in uptake was observed in the group fed the basal diet. In both groups the excretion was slightly increased during the first two wk. In the azo dye fed rats, the excretion decreased below normal at about the third week. The amounts of radioactive Rose Bengal excreted in the bile were proportional to the amount of azo dye excreted in the bile. (Author summary)

64-1717 ENZYMES OF GALACTOSE FORMATION IN NORMAL AND NEOPLASTIC MAMMARY GLAND. (E.) Shatton, J. B. (Fels Res. Inst., Temple U. Sch. Med., Philadelphia, Pa.), M. Gruenstein, H. Shay and S. Weinhouse. Pp. 33C-34C in Abstracts of Papers. 145th Meet. Am. Chem. Soc. New York, N. Y. Anderson, S. (Ed.), 1963.

As part of a continuing study on survival of functional activities through the neoplastic transformation, several enzymes of galactose synthesis were studied in normal rat mammary gland at various functional states, and in primary mammary tumors induced by 20-methylcholanthrene. Hexokinase was moderate, and showed little variation in the normal gland, but was high in tumors. UDPG dehydrogenase was completely absent from both tissue types.

In contrast, UDPG pyrophosphorylase was very low in nonpregnant, nonlactating glands; but increased 10-fold during late pregnancy and increased 100-fold during lactation. Likewise, UDPG-4-epimerase was barely detectable until late pregnancy and was very high during lactation. Both enzymes dropped precipitously after weaning. Both enzymes decreased markedly in the tumors of rats treated with estradiol. An anomalous result was obtained in mammary glands stimulated to growth and lactation by the Furth mammatropic pituitary tumor, or by estradiol or insulin. Despite the presence of lactose in the milk secreted by these glands, the epimerase was not detectable. The data thus suggest that a pathway for galactose synthesis exists not involving the isomerization of UDPG to UDPGal. (Author summary)

64-1718 RIBONUCLEIC ACID AND PROTEIN SYNTHESIS OF MOUSE EPIDERMAL CELL DURING EXPERIMENTAL CARCINOGENESIS AND IN CARCINOMA. (Ger.) Oehlert, W. (Inst. Path., Albert-Ludwigs-U., Freiburg i. Br., Germany) and B.v. Pein. Beitr. Path. Anat. 128(2):300-333, 1963.

Epidermal hyperplasia, papillomata and keratinized epithelial carcinoma were produced in male white mice by painting with 0.25% solutions of 20-methylcholanthrene in benzene. The albumin and RNA metabolism were measured by inj. of H^3 -leucine and H^3 -cytidine. There was a significant rise in albumin metabolism in the cytoplasm and in the RNA synthesis of the nucleus after a single treatment in all cells of the epidermis. In the course of this, the normal pattern of H^3 -leucine uptake in the stratified squamous epithelium, is lost. A further rise in the albumin and RNA synthesis was noted in papillomata and carcinomata. There was no change in the pattern of uptake of H^3 -cytidine by the nucleus even in fully formed cancer cells. The nucleolus is the site of max. uptake, as in the normal cell. While the relative rate of RNA synthesis--measured as the uptake of H^3 -cytidine in the precipitable RNA fraction--runs parallel with the increase in size of the nucleus in the papilloma, the RNA production in the cancer cell is greater than would be expected from the size of the nucleus. Albumin and RNA synthesis are greater in peripheral sections of the tumor than at the center or in keratinized tissues. The rise in metabolism of the epidermis during treatment with a carcinogen is ascribed to an action of the polycyclic hydrocarbon on the cytoplasmic proteins. The cause of the increase in cells which leads to the hyperplasia is discussed in relation to damage to the post-mitotic cells which may lose their ability to form mitosis-inhibiting substances. (Author summary)

64-1719 CLINICAL SIGNIFICANCE OF SYNTHETIC PROGESTEROIDS AND THEIR POSSIBLE ROLE IN CARCINOGENESIS. (Ger.) Tóth, F. (1st. Clin.

Gynec., Med. U. Budapest, Hungary). Zschr. Geburtsh. Gynaek. 161(1):94-102, 1963.

The author has performed studies in a total of 107 women who had been treated with synthetic progestroids. Excellent results could be achieved in various bleeding anomalies, in sterility and in endometriosis. As a biological anticonception agent, Lyndiol has proved to be most suitable. Furthermore, animal experiments were carried out in 85 infantile female rats. According to the results, the synthetic progestroids do not bring about an acceleration of carcinogenic processes. In animals continuously treated with hormones, it is emphasized that there was a nearly 4-fold increase in uterine wt. compared to normal, and diminution of lipoids in the fasciculate and the reticular zone of the adrenal cortical substance as well as the absence of corpora lutea in the ovaries. (Author summary)

54-1720 PART I. THE SYNTHESIS AND RESOLUTION OF ANTHRASTEROIDS. PART II. MODEL STUDIES FOR THE SYNTHESIS OF Δ -PIMARIC ACID. (E., Thesis, U. Microfilms, Ann Arbor, Mich., No. 63-5641.) Kulier, C. P. (U. Kansas, Lawrence, 1962). Dissertation Abstr. 24(2):516-517, 1963.

Because anthrasteroids may be involved as part of a biochemical pathway to endogenous carcinogens, a variety of anthrasteroids were synthesized for biological testing. Synthesis of Δ -pimaric acid described, the starting material of which was cholesterol.

54-1721 ACTIVATION OF TESTICULAR ADRENAL REST TISSUE BY PROLONGED EXCESSIVE ACTH PRODUCTION. (E.) Hamwi, G. J. (Ohio State U. Health Ctr., Columbus), G. Gwinup, J. H. Mostow and P. K. Besch. J. Clin. Endocr. 23(9): 861-869, 1963.

A case history is presented of a 14-year-old boy with Cushing's syndrome who had had subtotal adrenalectomy, subtotal resection of a chromophobe adenoma of the pituitary followed by partial hypophysectomy and left orchiectomy for a testicular tumor which had developed approx. 6 yr. after start of symptoms and which was believed to be an adrenal rest tumor produced by continuous excessive ACTH secretion.

54-1722 PAPER ELECTROPHORETIC STUDIES ON ENZYMES IN THE LIVER OF RATS FED Δ -DIMETHYLAMINOAZOBENZENE. VII. ASPARAGINASE. (E.) Sato, T. (Dept. Biochem., Showa Sch. Med., Tokyo), Y. Tamura and S. Kishi. Gann (Jap. J. Cancer Res.) 54(3):261-268, 1963.

Asparaginase activity in the liver of rats fed Δ -dimethylaminoazobenzene (DAB) was studied semiquantitatively by using paper electrophoresis and was represented in a pattern taking into

consideration the length of migration of the enzyme on the paper. Two prominent peaks were found in the pattern in the case of normal liver in the digests with pyruvate and phosphate added. One was the faster migrating part (peak I) and the other the slower part (peak II). The peaks I and II were confirmed as Greenstein's asparaginase I and II, resp., by analyzing the activation effect of phosphate and pyruvate, and also by heat treatment. The pattern of cirrhotic liver was almost similar to that of normal liver. In hepatoma, however, peak II remained very low and peak I was not seen. In rats fed DAB without interruption for 4 wk., peak I was lost completely, but peak II remained much as in the case of normal liver. After 11 wk. of the experiment, peak II became very low and the pattern resembled that of hepatoma. (Author summary)

64-1723 PAPER ELECTROPHORETIC STUDIES ON ASPARAGINASE IN THE LIVER OF RATS FED CARCINOGENS, AND IN THE FETAL AND REGENERATING LIVER OF RATS. (ADDENDUM) SIMILAR STUDIES OF MICE. (E.) Tamura, Y. (Dept. Biochem., Showa Sch. Med., Tokyo). Gann (Jap. J. Cancer Res.) 54(3):269-274, 1963.

The pattern of activity of liver asparaginase was investigated by paper electrophoresis, before and after feeding amino azo dyes. The dyes tested were 3'-methyl-4-dimethylaminoazobenzene, o-aminoazotoluene, and 4-aminoazobenzene. These chemicals were incorporated in the diet of rats on the same molar level as the 4-dimethylaminoazobenzene (DAB) used in an earlier paper (see CRA 1(9-10):#1722, 1964). 2-Acetamidofluorene was also used in the present experiment. Some of the chemicals affected the pattern of asparaginase activity, while the others gave no effect. Similar examinations were made with fetal and regenerating rat liver. The pattern of the former resembled that of hepatoma and of the latter to that of normal liver. Similar experiments made with mice fed with DAB in their early experimental days showed that the asparaginase activity was higher and more resistant to the chemical than was the case in rats. (Author summary)

64-1724 EFFECT OF PRETREATMENT WITH HEPATOTOXIC SUBSTANCES ON 2-ACETAMIDOFLUORENE AND INDOLE TUMORIGENESIS IN RAT. EFFECT OF CARBON TETRACHLORIDE AND DL-ETHIONINE. (E.) Oyasu, R. (Kokuritsu Kyoto Hosp., Japan). Gann (Jap. J. Cancer Res.) 54(3):339-351, 1963.

To study further the causal relationship between severe benign liver damage and bladder neoplasms, liver injury was produced in male rats by s.c. inj. of CCl_4 or feeding of an ethionine-containing synthetic diet. All rats were then fed synthetic diets containing 2-acetamidofluorene (AAF) or AAF and indole for up to 12 mo. The apparent hepatotoxicity of AAF was enhanced and all rats fed AAF

alone after pretreatment with CCl₄ died of severe hepatic damage within 66 days without tumors. Yet in rats fed AAF and indole, the previously demonstrated protective action of indole against hepatotoxicity of AAF was also enhanced providing a much more striking demonstration of protection by indole than was seen in the previous experiment. Pretreatment with CCl₄ decreased tumor incidence in all sites. The ethionine feeding preceding AAF and indole treatment also failed to increase tumorigenesis in the liver and bladder. Therefore, the present experiments did not confirm the postulated enhancement of AAF carcinogenicity by prior hepatic damage induced by CCl₄ or ethionine pretreatments. On the contrary, carcinogenic action of AAF may even have been diminished, at least in presence of CCl₄-induced cirrhosis, where a great diminution was observed. (Author summary)

- 64-1725 EXPERIMENTAL STUDIES ON THE RELATION OF MESENCHYMAL TISSUE TO THE DEVELOPMENT AND GROWTH OF THE TUMOR. (E.) Urabe, M. (Dept. Surg., U Kanazawa Sch. Med., Japan), T. Mizukami and S. Miyazaki. *Gann (Jap. J. Cancer Res.)* 54(3):353-363, 1963.

Development and growth of a tumor were examined when the mesenchymal tissue was damaged by admin. of drugs or by intervention of the nervous system, in order to clarify the relationship between the mesenchymal system and the tumor. When cortisone or Trypan Blue was admin. to a rat, foci in the lung which developed after intrabronchial inj. of carcinogenic substances (arsenious acid, 20-methylcholanthrene or 3,4-benzpyrene) tended to undergo malignant change more intensely than that of the control group. When the striate body of a rat was destroyed by electrocoagulation or inj. of a mercuric chloride soln., the growth of s.c. implanted Yoshida sarcoma was accelerated. Skin tumor induced by 9,10-dimethyl-1,2-benzanthracene developed more frequently on the leg of the mouse after the sciatic nerve was cut. Incidence of skin tumor became greater when cortisone or Trypan Blue was admin. in addition to cutting of the sciatic nerve. These experimental results showed that the development and growth of a tumor were promoted by damage of the mesenchymal tissue, assumedly due to the weakened defensive response of the living body against invasion of a tumor. (Author summary)

- 64-1726 INFLUENCES OF CARCINOGENIC SUBSTANCES ON MICROORGANISMS. IV. MUTAGENIC ACTION OF 4-NITROQUINOLINE-N-OXIDE ON T2 PHAGE. (E.) Pan, I. H. (Dept. Bact., Natl. Taiwan U. Coll. Med., Taipei). *J. Formosa Med. Assn.* 62(2):107-111, 1963.

T2 phage was treated with 4-nitroquinoline-N-oxide *in vitro*. Mutagenic action of the agent on the phage was checked by plaque morphology

mutation and host range mutation. From the results of this study, it was proven that: (1) This chemical could induce phenotypic plaque morphology mutation. (2) When *Shigella flexneri* 3b NIHJ strain was used as the host cell, plaque forming mutants were observed both in the control and the treated groups. The number of mutants formed in the latter group was significantly larger than that formed in the control group. (Author summary)

- 64-1727 PUROMYCIN INHIBITION OF ENZYME INDUCTION BY 3-METHYLCHOLANTHRENE AND PHENOBARBITAL. (E.) Conney, A. H. (Burroughs Wellcome & Co., Inc., Tuckahoe, N. Y.) and A. G. Gilman. *J. Biol. Chem.* 238(11):3682-3685, 1963.

The admin. of puromycin to rats completely blocked increases in the activity of aminoazo dye N-demethylase caused by 20-methylcholanthrene or phenobarbital, providing evidence for the synthesis of more enzyme protein. Phenobarbital and certain other inducers of the aminoazo dye N-demethylase system were potent stimulators of net synthesis of liver microsomal protein. (Author summary)

- 64-1728 THE FORMATION OF CARCINOGENIC NITROSAMINES FROM TISSUE AMINES AND INHALED NITROGEN OXIDES. (Ger.) Henschler, D. (Inst. Pharm., Julius-Maximilians-U., Würzburg, Germany) and W. Ross. *Naturwissenschaften* 50(14):503, 1963.

Tobacco smoke and industrial and urban air pollution are discussed as causes of the increase in lung cancer in civilized countries. Nitrosamines formed during smoking or through contact with suitable tissue amines have been suspected of carcinogenic action. However, preliminary results of experiments with the induction of lung tumors in mice by exposure to NO₂ indicated that the likelihood of the formation of carcinogenic nitrosamines from inhaled nitrogen gases and amino compounds by the respiratory tissues is very slight.

- 64-1729 THE EFFECT OF PROLONGED INHALATION OF LOW CONCENTRATIONS OF NITROGEN DIOXIDE UPON THE LUNGS OF MICE. (Ger.) Ross, W. (Inst. Path., U. Würzburg, Germany) and D. Henschler. *Naturwissenschaften* 50(14):503-504, 1963.

NMRI mice (female, 6-8-weeks old) were exposed to NO₂, 40 ppm. After exposure for 6-10 hr. the lung parenchyma reacted with massive edema of the septae; 14 hr. later, alveolar epithelium and septal cell elements started to proliferate; 48-52 hr. after the end of treatment, cellular proliferation was maximal, with vigorous desquamation of alveolar epithelium and atypical mitoses present even in the interstitial septae. Three

groups of survivors from this experiment were exposed to 40 ppm for 48 hr.: (1) 2x/wk.; (2) every 10th day; (3) every 30th day. After 15 mo. of such intermittent treatment the pulmonary reactions of the 3 groups were qualitatively similar. A total of approx. 14,000 serial bronchial sections showed that cell proliferations always started at the site of transition from bronchiolus to alveolus. Quantitatively, however, the reaction was least severe in the group with the most frequent exposure (group 1). In group 3, each exposure was followed by a progressively more severe reaction. Recovery was fastest in group 1. Cases of mild bronchitis and peribronchitis occurred in all 3 groups, but no pneumonia, bronchiolitis obliterans or lung fibrosis were observed.

64-1730 EXPERIMENTS ON THE INDUCTION OF CANCER IN RATS BY THE SIMULTANEOUS APPLICATION OF DIETHYLNITROSAMINE AND 4-DIMETHYLAMINO-AZOBENZENE. (Ger., Abstract) Schmähl, D. and C. Thomas. Zbl. Allg. Path. 104(9-11):578-579, 1963.

The hepatotropic carcinogens, diethylnitrosamine (DNA) and 4-dimethylaminoazobenzene (DAB) had a definite additive carcinogenic effect when applied simultaneously in albino rats at daily doses of 3 and 33 mg/kg, resp. When combined, the total carcinogenic dose for DNA was 445 mg/kg, that for DAB was 4,950 mg/kg whereas when admin. separately the doses were 720 and 7,500 mg/kg, resp. Thus only 60% of the usual carcinogenic dose was necessary when the agents were admin. simultaneously. Also, the latent period was shorter with combined application. DNA caused only hepatocellular carcinoma; DAB caused adenocarcinoma and liver cancer; despite the different tumor morphology, the cellular point of attack of both carcinogens was similar.

4-1731 THE ROLE OF 3,4-BENZOPYRENE IN EXPERIMENTAL TOBACCO CARCINOGENESIS. (E.) Roe, F. J. C. (Chester Beatty Res. Inst., London, S.W.3). Acta Un. Int. Cancr. 19(3-4):30-732, 1963.

When 1.25 µg 3,4-benzopyrene (BP) in 0.2 ml acetone was applied 3x/wk. to the dorsal skin of mice for 68 wk., a few transitory benign tumors but no malignant tumors appeared. However when mice were similarly treated with a

20% acetone soln. of cigarette smoke condensate which contained only 0.025 µg BP per 0.2 ml soln., malignant tumors as well as benign were seen. This result indicated that the carcinogenicity of cigarette smoke condensate for mouse skin could not have been due solely to its BP content. When BP was added to cigarette smoke condensate so as to increase its conc. to 1.25 µg in 0.2 ml, a mixture of high carcinogenic potential was produced. These findings are consistent with the suggestion made earlier that there are cocarcinogenic components in smoke condensate which can magnify the carcinogenic effect of BP. (See also CRA 1(8):#1470, 1963.) (Author summary)

64-1732 DISTRIBUTION OF 20-METHYLCHOLANTHRENE IN ORGANS OF METHYLCHOLANTHRENE-INDUCED LEUKEMIC MOUSE. (Jap.) Sezaki, T. (Dept. Int. Med., Okayama U. Sch. Med., Japan), M. Susaki and S. Irino. Igaku To Seibutsugaku (Med. Biol.) 67(2):65-71, 1963.

RF strain mice with leukemia induced by admin. of 20-methylcholanthrene (20-Me), were studied to determine the distribution of the carcinogen in various organs and at various developmental stages of the disease. High conc. were observed in the thymus and blood forming organs, especially the bone marrow. On the basis of these experimental results, the relationship between the pathogenesis of leukemia and 20-Me distribution was discussed.

64-1733 THE DIET OF RATS DURING LIVER TUMOR INDUCTION WITH N-DIMETHYLAMINO-AZOBENZENE. (Rus.) Bykorez, A. I. (Ukrainian Res. Inst. Exptl. Clin. Oncol., Kiev, USSR). Vop. Onkol. 9(11):15-18, 1963.

Feeding 32 random bred female white rats (120-150 g) with cod liver oil, carrots, and rice in addition to dimethylaminoazobenzene (12 mg in 1 ml cod liver oil) produced malignant tumors of the liver in 24/32 (75%) during a period of 5.5 mo. Macroscopically they were nodes 2-3 cm in diameter and of a yellowish hue. Metastases were found in the omentum in 2/24, in the lung, in 1/24. Morphologically, the tumors were mainly cholangiocellular cancer of the adenocarcinoma type. The hepatocellular type was rare and, as a rule, was accompanied by cirrhosis in all the rats.

See also abstract nos.: 1633, 1636, 1637, 1646, 1653, 1655, 1657, 1658, 1659, 1758, 1771, 1778

VIRAL CARCINOGENESIS

- 64-1734 STUDY ON THE INTERRELATIONSHIP BETWEEN TUMOR VIRUS AND TUMOR CELL IN MAMMARY CANCER AND LEUKEMIA OF MOUSE. (Jap.) Awano, G. (Fukushima Pref. Med. College, Fukushima, Japan), S. Tojimer, S. Matsuyama, K. Takahashi and H. Sato. Nippon Naika Gakkai Zasshi (J. Jap. Soc. Intern. Med.) 51(12): 47-48, 1963.

As determined with the use of the electron microscope, in breast cancer and leukemia of the mouse, tumor virus was observed both intra- and extracellularly but not in the nucleus. In leukemia the virus is commonly observed mostly on the outer surface of the cell wall, while some is observed in the intracellular space. However, in breast cancer, virus is commonly observed in the intracellular space or vacuoles; growth is not limited to the outer part of the cell. The virus of mouse leukemia became difficult to detect after it had been transplanted for a long time.

- 64-1735 EXPERIMENTAL INVESTIGATIONS IN MURINE LEUKEMIA. V. ISOLATION OF CYTOPATHOGENIC AGENT FROM MURINE LEUKEMIC PRODUCTS OBTAINED FROM LINE C₅₇ MICE AND MAINTAINED IN VITRO ON HUMAN EMBRYO CULTURES. (Rum.) Nastac, E. (Inst. Inframicrobiol., Rumanian Acad. Sci., Bucharest), M. Lungu, G. Dona and G. Rutter. Stud. Cercet. Inframicrobiol. 14(2):155-159, 1963.

Previously trypsinized cultures of human embryonic tissue were inoc. with 0.2 ml of a 1:10 suspension of brain tissue (A) or with a mixed suspension of liver and spleen tissue (B), removed from a C₅₇ mouse (weakly leukemogenic strain) with spontaneous lymphatic leukemia, or with a suspension of chorioallantoic membrane from an 8-day-old chick embryo previously inoc. (4 successive passages) with leukemic blood (C) from the same mouse. Successive passages were then carried out using cell-free culture fluid after freezing-defrosting 3 times at the time of max. cytopathogenic effect. (A) and (C) produced similar cytopathogenic effects which appeared at 48-72 hr. after inoc. and started in the peripheral zone then expanded to the whole culture and reached a max. after 5-6 days. These effects were transmissible for (A) and (C) up to the 17th and 12th passage, resp. (experiments were still continuing at the time of publication). Modifications in the cellular morphology consisted of abnormal fibroblasts which gradually became round, large cells with a tendency of gathering in small clusters; appearance of giant, polynucleated cells, also gathered in small groups (2, 3 or 4) and a discontinuous aspect of the culture with alternating zones of normal and degenerated cells. The degenerative process involved the nucleus and cytoplasm. Inoculation of (B) produced a cytopathogenic effect trans-

missible up to the 6th passage only (no further details). An attempt at reinoculation of the cytopathogenic agent on the chick chorioallantoic membrane gave inconclusive results. The authors state that further experiments (inoc. to animals) will demonstrate if the cytopathogenic agent isolated is responsible for the appearance of spontaneous leukemia in the C₅₇ mouse.

- 64-1736 EXPERIMENTAL INVESTIGATIONS IN MURINE LEUKEMIA. NOTE VI. EXPERIMENTAL AND HISTOPATHOLOGIC STUDY OF DEVELOPING CHICK EMBRYOS INOCULATED WITH MURINE LEUKEMIA PRODUCTS OF LINE C₅₇. (Rum.) Nastac, E. (Inst. Inframicrobiol., Rumanian Acad. Sci., Bucharest), G. Balmus, G. Popescu, G. Rutter and M. Lungu. Stud. Cercet. Inframicrobiol. 14(4):417-426, 1963.

Inoculation into the chorioallantoic membrane (CM) of suspensions of blood, liver, and spleen from mice with lymphatic leukemia, appearing spontaneously in mouse line C₅₇ (slightly leukemogenic), produced death of the embryos in about 70% of the cases and serially transmissible histopathologic lesions. The lesions observed following inoc. of the above products affected both the CM and the embryo, more accentuated on the former; the type of the lesions was especially of a proliferative and infiltrative type. These lesions were caused by an agent of a viral nature, transmissible in series, which grew in human embryo cell cultures in vitro. The higher infectivity of the liver and spleen suspensions as compared to that of the blood is demonstrated by the number of blind passages necessitated for adapting the virus to the chick embryo and the greater intensity of the lesions produced by the suspensions in the CM and the embryos. These findings plead in favor of the viral nature of mouse C₅₇ leukemia. (Author summary)

- 64-1737 ELECTRON MICROSCOPY OF MYXOMA VIRUS. (E.) Chapple, P. J. (Fisheries Food, Infest. Control Lab., Worplesdon, Surrey, England) and J. C. N. Westwood. Nature (London) 199: 199-200, 1963.

Electron microscopic findings in rabbit kidney cells infected with myxoma virus are reported. In addition to the similarities in size, shape and fine structure revealed by negative staining, recent work has demonstrated a fundamental serological relationship between the myxoma-fibroma group of viruses on one hand and the vaccinia-ectromelia group on the other. On the present evidence, therefore, the myxoma-fibroma viruses may be included with confidence as a subgroup of the pox viruses.

- 64-1738 NUCLEOTIDE SEQUENCE INVESTIGATIONS IN MICROSOMAL RIBONUCLEIC ACIDS OF NORMAL

AND ROUS SARCOMA VIRUS-INFECTED TISSUES. (E.)
Delihas, N. (Med. Res. Ctr., Brookhaven Nat.
Lab., Upton, N. Y.) and E. Evans. Nature (London)
199:488-489, 1963.

No significant differences could be observed by
ion exchange chromatography of pancreatic RNase
digests between microsomes from normal chick
chorioallantoic membranes and from Rous sarcoma
virus-infected membranes. It is suggested that
Rous sarcoma virus RNA may be present in amounts
too small to be detected by the present method
of analysis.

64-1739 CELL MORPHOLOGY AND ENZYME CHEMISTRY
IN EXPERIMENTAL LEUKEMIA. NOTE 1.
SOME PRELIMINARY OBSERVATIONS ON HUMAN AND
EXPERIMENTAL LEUKEMIA. (Rum.) Lupu, N. G.
(Inst. Int. Med., Rumanian Acad. Sci., Bucharest),
Micu, E. Mihailescu, S. Maximilian, P. Grozea,
Gociu and E. Sighetea. Stud. Cercet. Med.
Intern. 4(3):387-391, 1963.

Cytomorphologic, cytochemical and enzyme studies
were carried out in more than 400 pts. with
chronic or acute leukemias. Similar investiga-
tions were undertaken in approx. 100 mice (1-2-
day-old; RAP strain) with experimental leukemia
induced by i.p. inj. of noncellular human bone
marrow filtrate, taken from subjects with leu-
kemia. Some of the cytomorphologic changes
(no details) seen in humans were similar to those
encountered in mice and permitted classification
of the experimental leukemias according to the
terminology used for human leukemia; differences
and similarities observed in the field of cyto-
chemical and cellular enzymes, regarding m-oxi-
dases (probably cytochrome oxidases), peroxidases,
alkaline and acid phosphatases, and especially
RNA, glycogen as well as other cellular components,
are stressed. The similarities observed, brought
forward the problem of a common origin for the
two types of disease. The differences seen appear-
ed to indicate the possible association with other
factors, which, at the present time are of an un-
known nature. Also, various types of leukemia
viruses may exist which are capable of producing
diversified lesions.

64-1740 SPECIFIC ADENOVIRUS COMPLEMENT-FIXING
ANTIGENS IN VIRUS-FREE HAMSTER AND
RAT TUMORS. (E.) Huebner, R. J. (NIH, Bethesda),
P. Rowe, H. C. Turner and W. T. Lane. Proc.
Nat. Acad. Sci. USA 50(2):379-389, 1963.

Type-specific complement-fixing antigens were
demonstrated in cancers induced in hamsters by
adenovirus (AD) types 12 and 18, and in rats by
type 12. Primary and transplanted tumors
were found to be devoid of infectious virus in
over 50 separate tests. The specific CF tumor
antigens occurred with remarkable regularity in
transplanted types 12 and 18 tumors and in serial
tissue cultures of type 12 hamster tumor cells.

The tumor antigens were not sedimentable and were
found to have other properties similar to type-
specific or "C-soluble" antigens produced in tissue
cultures during replication of adenoviruses 12 and
18. Antibodies induced in hamsters and rats
carrying primary tumors and serial transplants
of tumor cells reacted with type-specific viral
antigens produced in KB and HEK tissue cultures
by replicating AD types 12 and 18. The continuous
presence of type-specific viral-like antigens in
the absence of the virus itself provided high-
order evidence in favor of the conclusion that
they were coded for by viral information incor-
porated in the genetic apparatus of the cancer
cells. Complement-fixing antigens were also
found in hamster tumors produced by the SV40
virus and the Schmidt-Ruppin variant of avian
Rous virus. These virus-like tumor antigens,
like the AD antigens, could not be accounted for
by demonstrable infectious virus. The presence
of specific virus-related antigens in hamster and
other animal tumors induced by 3 different groups
of viruses (adenovirus, papovavirus, and avian
leucosis) suggested that similar antigens might be
demonstrable in some naturally occurring "virus-
free" tumors of animals and man. (Author summary)

64-1741 ON SOME APPARENTLY NONTUMORIGENIC
VIRUSES ISOLATED FROM TRANSPLANTABLE
TUMORS OF THE RAT. (It.) Albano, A. (Inst.
Hygiene, Virol. Ctr., U. Milan, Italy) and
S. De Donato. Boll. Ist. Sieroter. Milan
41(11-12):590-598, 1962.

A viral agent has been isolated repeatedly from
2 transplantable tumors: Yoshida hepatoma and
Walker adenocarcinoma. The agent was found to
grow in KB cells, monkey kidney cells (primary
and continuous lines), rat or mouse embryonic
tissues, and rat ascites myeloma. The agent is
filterable through EKS Seitz filters, is not
inactivated at 56°C for 30 min., is inactivated
by acetone and ether, agglutinates strongly mouse
and rat erythrocytes, less strongly those of
guinea pigs, rabbit, chicken or man. The virus
is nonpathogenic to adult and newborn mice and
guinea pigs. It is nonantigenic to mice and rats,
while it is strongly antigenic to the guinea pig,
and is not neutralized by anti-polyoma sera. The
main cytopathic effect of the virus is formation
of syncytia.

64-1742 ON THE ANTIGENIC AND ETIOLOGICAL
SIMILARITIES BETWEEN NEORICKETTSIOSIS
AND MALIGNANT CHRONIC RETICULOSES WITH SPECIAL
REFERENCE TO LYMPHOGRANULOMATOSIS (MORBUS HODGKIN).
(Bul.) Kuindziev, I. (Inst. Microbiol., Bulgarian
Acad. Sci., Sofia). Izv. Mikrobiol. Inst. (Sofia)
14:119-126, 1962.

As in the author's preceding investigation in which
a close antigen relationship was established be-
tween the causative agents of ornithosis-psittaco-
sis on the one hand and that of lymphogranulomatosis

on the other hand, now in serological investigations using the complement fixation test and the conglutinating complement absorption test (C. C. A. T.), in the presence of an ornithosis-psittacosis antigen, the author has found 100% positive reactions to both tests in all 58 blood sera investigated from people actually having lymphogranulomatosis (Morbus Hodgkin). This result likewise gives the possibility of making a serodiagnosis of Hodgkin's disease by the two methods mentioned above and using an ornithosis-psittacosis antigen. When inoculating white mice with blood from individuals with lymphogranulomatosis, all inoc. mice die. Their internal organs and brain reveal elementary corpuscles, and in the liver one observes Sternberg's giant cells. These experiments confirm the view about the virus etiology of lymphogranulomatosis, and an antigenic relationship is established between the causative agent of ornithosis-psittacosis and that of lymphogranulomatosis (Morbus Hodgkin) confirmed also by the experimental investigations which are the subject of the present work. (Author summary)

- 64-1743 RECENT STUDIES ON THE ELECTRON MICROSCOPY OF ONCOGENIC VIRUSES. (Fr.) Granboulan, N. (Inst. Sci. Res. Cancer, Villejuif (Seine), France). Bruxelles Med. 42(44): 1299-1313, 1962.

Electron microscopic studies are reported of tissues from AKR mice with spontaneous leukemias and lymphomas. In 21/24 animals examined, many organs, and especially the thymus, contained irregularly spherical particles about 98 m μ in diameter situated in the extracellular space and consisting of an external membrane and of a nucleoid. The relationship of these particles to the cell membrane was consistent with a type C classification, and in no case could an intracellular viral precursor be demonstrated. In some of the lymphoid leukemias studied, regardless of the presence or absence of extracellular virus, there were also nucleolar condensations and chromatin marginations. In spontaneous lymphomas of Swiss mice and also in transplanted lymphomas the viral particles are always intracellular, and form a large inclusion body. The particles are 70 m μ in diameter, contain no nucleoid, and instead consist of 2 concentric membranes similar to those of mammary tumors in mice. At the present time the particles found in lymphomas of Swiss mice have not been proven to be the etiologic agent by biological methods. Other studies reported are on the developmental cycle of SV40 in *in vitro* cultures of *Cercopithecus Aetiops Sabaeus* kidney. The earliest change in infected cultures is hypertrophy of the nucleus at about 12 hr. Between 12-48 hr. the number of viral particles increases, filling the nucleus, and replacing the chromatin, often forming crystalline structures. The virus particles measure 33 m μ , are spherical, with a centrally dense region, no membrane, but a clear

halo, probably representing the capsid. Gross nuclear and nucleolar changes appear to accompany viral multiplication. Other studies are reported, briefly, primarily dealing with cytochemical and autoradiographic technics in the electron microscope study of adenovirus 5, reo virus type III, polyoma, and SV40 multiplication.

- 64-1744 TRANSFORMATION OF BOVINE TISSUE CULTURE CELLS BY BOVINE PAPILLOMA VIRUS. (E.) Black, P. H. (Natl. Inst. Allergy Infect. Dis., Bethesda), J. W. Hartley, W. P. Rowe and R. J. Huebner. Nature (London) 199:1016-1018, 1963.

The diploid cell line of fetal bovine conjunctiva (strain DBC) inoc. with 20% extracts of 3 bovine papillomata showed consistent, distinct morphological changes within 3-10 days. On serial passage, the morphological changes were maintained. Cultures infected with a 10⁻³ dilution of the most potent wart extract grew out as normal appearing epithelial cells but by day 5 or 6 they underwent the characteristic change. That the agent responsible for the transformation was actually the bovine papillomata virus was indicated by serological data, chloroform resistance, filterability and sedimentability of the agent; and by the occurrence of positive results with wart extracts from cattle in 3 geographical areas.

- 64-1745 MALIGNANT NEOPLASMS INDUCED IN RATS BY EXTRACTS FROM HUMAN SARCOMATOUS TISSUE. (E.) Ageenko, A. I. (Hertzen State Oncol. Inst., Virol. Lab., Moscow). Folia Biol. (Praha) 9(1): 20-26, 1963.

See CRA 1(5):#846, 1963.

- 64-1746 GROWTH CURVES, HISTOLOGY AND VIRUS TITERS IN ROUS SARCOMAS. A COMPARISON BETWEEN PROGRESSIVELY GROWING AND REGRESSING TUMOURS. (E.) Stenkvist, B. (Dept. Path., U. Uppsala, Sweden) and J. Pontén. Acta Path. Microbiol. Scand. 58(3):273-282, 1963.

A dilution of Rous sarcoma virus was inoc. into both wings of 36 chickens. The volumes of the ensuing tumors were estimated from repeated measurements of the diameters. Serial biopsies from the tumors were assayed for virus and examined histologically. The material was divided into two main groups: progressive lethal tumors and regressing tumors. No significant differences with respect to growth rate, content of virus and histology was found between progressively growing tumors that later regressed and those which continued to progress. Tumors in a regressing phase showed an increased infiltration of lymphocytes, hemorrhages and necrosis, and in advanced stages, fibrosis. They contained no infective virus or very little. The findings are compatible with the hypothesis that sustained progressive growth of Rous tumors is normally

ly possible if normal cells are continuously converted" into Rous cells by released virus. (Author summary)

4-1747 VIRUS OF AVIAN MYELOBLASTOSIS (BAI STRAIN A). XXIV. NUCLEOTIDE COMPOSITION OF THE PENTOSE-NUCLEIC ACID AND COMPARISON WITH STRAIN R (ERYTHROBLASTOSIS). (E.) Bonar, R. (Dept. Surg., Duke U. Med. Ctr., Durham, N. C.), R. H. Purcell, D. Beard and J. W. Beard. Nat. Cancer Inst. 31(3):705-716, 1963.

Analyses were made of the nucleotide composition of the pentosenucleic acids of the BAI strain A (myeloblastosis) and strain R (erythroblastosis) avian tumor viruses purified from the blood plasma of birds with myeloblastosis and erythroblastosis, resp. The BAI strain A differed from strain R especially in the content of guanylic acid. There was a still greater difference between these agents and the Rous virus from tissue culture studied by other investigators. The nucleotide composition of strains BAI A, R, and virus obtained from these sources differed greatly from the analogous constitution of myeloblasts and other avian cells as well as that of Rous virus preparation from solid tissue tumors. Concentrates from normal chicken plasma did not contain pentosenucleic acid in amounts sufficient to detract from the results with the BAI A and R strains. The findings suggest real differences between these avian tumor virus strains in biochemical constitution. (Author summary)

4-1748 MULTIPLICITY OF CELL RESPONSE TO THE BAI STRAIN A (MYELOBLASTOSIS) AVIAN TUMOR VIRUS. VII. ELABORATION OF VIRUS BY NON-NEOPLASTIC HEPATIC CELLS. (E.) De Thé, G. (Dept. Surg., Duke U. Med. Ctr., Durham, N. C.), T. Ishiguro, D. Beard and J. W. Beard. J. Nat. Cancer Inst. 31(3):717-729, 1963.

Virus-particle elaboration by budding in microvilli of liver parenchymal cells at the bile canalicular border occurred in birds with extensive hepatic lymphomatosis induced by i.v. inoculation of BAI strain A virus. Canalicular lumen contained virus particles but no buds in chickens with myeloblastic leukemia. Neither buds nor particles were associated with the canaliculi in liver with extensive lymphomatosis following transplantation with nephroblastoma tissue and with small localized lymphoid cell deposits. Budding and canalicular particles seemed related to virus conc. in the invading lymphoid tissue or in the circulating blood plasma in myeloblastosis. (Author summary)

4-1749 ISOLATION OF A TYPE I ADENOVIRUS FROM A MALIGNANT CERVICAL ADENOPATHY. (Fr.) Phier, R. (Lab. Hygiene, Fac. Med., U. Lyon, France), Y. Chardonnet and M. Prunieras. Presse Med. 71(36):1733-1734, 1963.

An adenovirus of type I was isolated from a malignant cervical adenopathy, without the opportunity of obtaining a blood sample which would permit search for the possible presence of antibodies against this virus. Arguments are given against the hypothesis of an accidental contamination during withdrawal of a blood sample, or during the implantation of the tumor in the cell cultures. It is possible that this is a case of latent infection, comparable with that which is seen in glandular proliferation. Since it seems not to have been observed before in malignant cervical adenopathies (at least not to our knowledge), it warranted a report. Since certain adenoviruses have induced tumors after their inoc. into animals, we wondered whether this adenovirus--though of a different antigenic type from the one with oncogenic capacity--might have played a part in the formation of the malignant adenopathy. At present this question cannot be answered. (Author summary)

64-1750 ETIOLOGIC INVESTIGATIONS IN HODGKIN'S DISEASE. III. ATTEMPTS AT ADAPTATION TO LABORATORY ANIMALS OF THE AGENT ISOLATED IN CHICK EMBRYOS. (Rum.) Cajal, N. (Inst. Inframicrobiol., Rumanian Acad. Sci., Bucharest), M. Cepleanu, A. Schächter, Y. Sorodoc, R. Demetrescu and V. Lotreanu. Stud. Cercet. Inframicrobiol. 14(4):409-416, 1963.

Eleven identical viral strains were isolated in embryonated chicken eggs, inoc. by the intra-amniotic route with products from cells of pts. with Hodgkin's disease; subsequently, 5 of these strains were adapted to the white mouse, after intranasal inoc. A constantly lethal disease, with an incub. of 4 to 5 days, was obtained with the mouse-adapted virus following intranasal, i.p., intracerebral, i.m., s.c. and i.v. inoc. The virus was detected in most of the organs of the animals which died of the experimental disease. Complement fixation tests with the use of a heat-inactivated antigen from the lungs of these mice revealed that the antigen behaved similarly to the antigen prepared from the chicken embryos.

64-1751 SEARCH FOR VIRUS IN HUMAN LEUKEMIA: EFFECTS OF NUCLEIC ACIDS EXTRACTED FROM LEUKEMIC TISSUES ON CELL CULTURE. (E.) McAllister, R. M. (Dept. Ped., U. Southern California Sch. Med., Los Angeles) and G. D. Hammond. J. Nat. Cancer Inst. 31(6):1549-1557, 1963.

Nucleic acids, extracted by the phenol method from 18 normal tissues and 56 leukemic tissues, were inoc. into cell cultures of human amnion, human fetal skin muscle and kidney, human bone marrow, and monkey kidney. No reproducible cytopathic or transforming effects were observed in the inoc. cultures. Control studies with infectious poliovirus ribonucleic acid (RNA) suggested that the optimal conditions for cell infection used in these experiments and the cell

numbers extracted should have allowed detection of each cell had it contained one infectious RNA molecule per cell and if such a molecule produced a clone of transformed cells or a cytologic change. The negative results obtained would appear significant if the hypothetical human leukemia viruses were RNA-containing viruses. Similar control studies with infectious deoxyribonucleic acid (DNA) extracted from SV40 indicated that an infectious DNA would have been much more difficult to detect. Such results may be interpreted as a failure of the methods employed, rather than as evidence against the possible viral etiology of human leukemia. (Author summary)

- 64-1752 DIFFERENCES AMONG THE SOLUBLE ANTIGENS OF MYXOMA VIRUSES ORIGINATING IN BRAZIL AND IN CALIFORNIA. (E.) Reisner, A. H. (Dept. Zool., Sydney U., Australia), W. R. Sobey and D. Conolly. *Virology* 20(3):539-541, 1963.

In a study of the soluble antigens of myxoma viruses of different origins it is reported that Brazilian strains (Lausanne and Standard Laboratory strains and their derivatives) and California strains (M.S.W. and California Nov. 59) and their derivatives exhibited different serological properties. The derived strains, however, showed no differences from the parent strain. Fibroma Boerlage showed weak cross reaction with both Brazilian and California strains (and derivatives) but was different from both. Three of the variants of the Brazilian virus (Glenfield virus, K.M. 13 and Uriarra) were field variants appearing in Australia in a different host (*Oryctolagus cuniculus*) than in Brazil (*Sylvilagus brasiliensis*); the point is made that despite this the antigenic structure did not change.

- 64-1753 POTENTIATION OF THE ONCOGENIC ACTION OF A TUMORAL VIRUS BY ITS ASSOCIATION WITH VACCINIA VIRUS. (E.) Ilie, B. *Rumanian Med. Rev.* 7(2):73-74, 1963.

The original paper appeared in the Rumanian language in *Oncologia si Radiologia*, No. 3, 1962. When cell-free filtrates of Guerin's tumor or fluid from Ehrlich's ascites were inoc. separately into the chorioallantoic membrane of chick embryos, poorly developed proliferative changes were observed on the chorioallantois. However, when the materials were inj. in association with vaccinia virus, intense proliferative alterations of the chorioallantois were observed, involving the ectoderm and the mesoderm. In addition, the destructive phase of the vaccinia virus was avoided. In some cases the chorioallantois from eggs inj. with Ehrlich ascites + vaccinia virus also showed small surface tumors, consisting of pluristratification of the ectoderm, and marked thickening of the mesoderm where proliferation was massive and polymorphous. The lumen of

blood vessels contained plasmodia and numerous mononuclear cells. When filtered ascitic fluid was inj. into mice in association with vaccinia virus, a higher frequency of tumor ascites was observed than when filtrates were inj. alone.

- 64-1754 SURFACE MUCOPOLYSACCHARIDES OF POLYOMA VIRUS TRANSFORMED CELLS. (E.) Defendi, V. (Wistar Inst., Philadelphia, Pa.) and G. Gasic. *J. Cell. Comp. Physiol.* 62(1): 23-31, 1963.

Hamster embryo cells transformed *in vitro* by polyoma virus showed a thick coat of acid mucopolysaccharides (sialo-mucin) as determined by a Mowry's modification of the Hale's reaction following neuraminidase treatment. The intensity of the reaction varied in the cell lines tested, even though it was relatively constant for each cell line during the period of observation, and it could be correlated with the degree of contact inhibition exhibited by these cells *in vitro*. It is suggested that the increase of sialo-mucin at the surface of the transformed cells is one of the main factors responsible for the loss of contact inhibition. (Author summary)

- 64-1755 ULTRASTRUCTURE OF A VARIANT OF THE FURTH MOUSE MASTOCYTOMA. (Ger.) Sellyei, M. (1st. Inst. Path. Anat., Exp. Cancer Res., Med. U. Budapest, Hungary) and H. David. *Zschr. Mikr. Anat. Forsch.* 70(1):103-117, 1963.

On the basis of electron microscopic investigation of a variant of the Furth mastocytoma growing in random bred white mice, the mast cell granules were seen to originate by means of condensation of material in the ground substance and in the canaliculi of the endoplasmic reticulum. The contraction of the granule substance, the increase in electron density, and the vesicular transformation could be considered as secretory phenomena. These processes are further increased after s.c. admin. of protamine sulfate. In the cytoplasm of the tumor cells, virus-like particles may be found. (Author summary)

- 64-1756 STUDY OF TOXIC FACTORS ASSOCIATED WITH MOUSE MAMMARY CARCINOMAS IN EGG CULTURES. (E., Thesis, U. Microfilms, Ann Arbor, Mich., No. 63-5274). McDuffie, N. G., Jr. (U. Texas, Houston, 1962). *Dissertation Abstr.* 24(2):496, 1963.

Electron microscope studies made on mouse mammary carcinomas resulted in discovery of a buildup of virus-like particles upon culture of these tumors in chicken eggs. These particles occurred in the cytoplasm and intracellular spaces of the egg-grown tumors and were of three different types: (a) vesicular-type particles characterized by concentric double membranes with 65-80 m μ outer, and 30-40 m μ inner diameters; (b) particles

consisting of a dark nucleoid of 30-40 mμ diameter, surrounded by a single membrane 65-80 mμ in diameter; (c) bodies consisting of type (a) or type (b) particles enclosed in a thin outer membrane about 100-300 mμ in diameter. The majority of particles seen were of type (a). Only a few type (c) particles were found. Morphologically these three types of particles were similar to those which have been associated with the Bittner leukemia factor by other workers; yet the chance that they were chicken viruses has not been ruled out entirely. It is likely, however, that they were derived from the tumor tissue and that their increase in number resulted from lack of inhibition in the eggs as compared to the host mice. These particles appeared to be produced by budding of the endoplasmic reticulum of the cells. They were connected with toxicity which the transplanted tumors developed for chick embryos and which was preserved by culture of the toxic agents in eggs free from tumors. This toxicity was caused by particulate organisms in the virus size range, and since virus-like particles of type (a) and type (b) were found in the toxic egg fluids, they were assumed to be the toxic agents. Toxic egg fluids were inj. into newborn C57BL mice, but no tumors resulted in these mice before they reached one year of age. This did not disprove the theory that these were tumor viruses, however, because the C57BL mice are resistant to mammary tumor induction. This resistance might be especially pronounced for egg-adapted tumor viruses. On the basis of the results of this study, egg culture is suggested as a means for growth and study of animal and human tumors, especially for preliminary isolation of possible oncogenic viruses. (Author summary)

64-1757 AN ELECTRON MICROSCOPIC STUDY OF LEUKEMIA INDUCED IN RATS WITH GROSS LEUKEMIA. (E.) Okano, H. (Francis Delafield Lab., Columbia U., New York), A. Kunita and J. Furth. Cancer Res. 23(8):1169-1175, 1963.

The leukemia virus of Gross was adapted to W/Fu rats to which it became as highly pathogenic as in mice. The lymphomas produced in rats were variably thymic with or without leukemia and involvement of other organs. An electron microscopic study was made of the abundance of virus in the blood and various organs. Virus was found most often (100%) and in greatest abundance in the thymus. The earliest clearly recognizable change was "budding" on the plasma membrane associated with accumulation of virus between all preserved cells. At an advanced stage of the disease, cytopathic changes were evidenced by dissolution of the plasma membrane, innumerable

able viral particles intermingling with mitochondria, and other cytoplasmic elements. Intracellular viral particles were abundant in vesicles or canals and specific granules of megakaryocytes of the spleen and bone marrow, and few elsewhere in their cytoplasm. Conventional electron micrographs give no clue as to the primary site and mode of replication of viral nucleic acids. The viral particles seen resembled those of other leukemias. Some possessed tail-like structures as first described by Dalton for the Moloney virus. By fractionation of the blood plasma a nearly pure preparation of viral particles was obtained. This procedure was adapted to the thymus by dissociation of thymic cells by treatment with trypsin (instead of homogenization), followed by fractional centrifugation. The abundance of virus and the neoplastic transformation of lymphocytes in the thymus may be related to the presence of a specific factor in this organ. (Author summary)

64-1758 CELL-FREE TRANSMISSION OF 20-METHYLCHOLANTHRENE-INDUCED RF MOUSE LEUKEMIA AND ELECTRON MICROSCOPIC DEMONSTRATION OF VIRUS PARTICLES IN ITS LEUKEMIC TISSUE. (E.) Irino, S. (Dept. Intern. Med., Okayama U. Med. Sch., Japan), Z. Ota, T. Sezaki, M. Suzuki and K. Hiraki. Gann (Jap. J. Cancer Res.) 54(3):225-237, 1963.

The role of virus in the leukemia induced by 20-methylcholanthrene (20-Me) by skin painting of RF mice (see CRA 1(8):#1467, 1963) was investigated. Inoculation of cell-free filtrate from 20-Me-induced lymphocytic and myelogenous RF mouse leukemia into newborn mice of the same strain produced lymphocytic leukemia in 4 of 13 inoc. mice. Serial cell-free passage of the leukemia was also successful and the third passage is now in progress. Virus particles were observed by electron microscopy in the lymph node of 20-Me-induced leukemic mice. From these facts, the authors conclude that the chemical carcinogen induces leukemia by activating a latent virus naturally resident in the RF mice.

64-1759 INDUCTION OF SARCOMA IN DUCKS BY THE FOWL TUMOUR VIRUS. (E.) Thurzo, V. (Inst. Cancer Res., Bratislava, CSSR) and J. Smida. Neoplasma (Bratisl.) 10(4):445-447, 1963.

Using both partially purified and cell-free preparations of B77 fowl sarcoma virus and the Bryan strain of Rous sarcoma virus (obtained by inoc. of 6-11-day-old white leghorn chicks) tumors were developed in 34/34 day-old White Peking ducks with the first virus strain, but in 0/20 with the Bryan strain. (See also CRA 1(5):#907, 1963.)

See also abstract nos.: 1638, 1639, 1640, 1641, 1642, 1644, 1645, 1647, 1648, 1650, 1652, 1654, 1656, 1662, 1663, 1690, 1691, 1702

- 64-1760 OBSERVATIONS ON THE TRAUMA-TUMOR RELATIONSHIP IN THE LIGHT OF A CASE OF MALIGNANT MELANOMA ARISING ON A TOE AT THE SITE OF TRAUMA. (It.) Pedrocchi, A. (Clin. Orthoped., U. Torino, Italy). Minerva Ortop. 14(6):273-278, 1963.

A case is described of a man (age 51) who during 6 mo. after a brick injured a toe, was subjected to disarticulation in 2 stages, the last time because of a granulomatous lesion and appearance of large inguinal adenopathies. Less than a mo. later several small non-tender nodules appeared between the second and third metatarsals, and at that time resection of inguinal adenopathies revealed metastatic melanoma. The small lesions were later found to be due to melanoma. The pt. died 14 mo. after the original trauma, in spite of intensive roentgen and cytostatic treatment.

- 64-1761 EPITHELIOMAS OF ARSENICAL ORIGIN. (Fr.) Tello, E. E. (Dept. Derm., Fac. Med. Sci., U. Cordoba, Argentina). Laval Med. 34(6): 762-768, 1963.

The author reports on his experience with cutaneous arsenical epitheliomas which he believes to exist at the present time only in the province of Cordoba in Argentina. The geographic distribution of these tumors is due to the fact that the waters of this region, which come from artesian wells of the upper stratum, contain a considerable amount of arsenic or arsenical salts. A large number of pts. were observed with manifestations of arsenical toxicity which consisted of histological lesions of apparently normal skin, symmetric palmo-plantar keratoderma and sometimes, melanoderma. Arsenical epitheliomas arise on these chronic arsenical dermatoses and are characterized by various clinical and histological forms and lie asymmetrically, preferably in covered regions. The author points out, on the basis of 175 cases, that Bowen's disease and multiple superficial epitheliomatosis only exceptionally occur in individuals without signs of chronic arsenical dermatosis; this confirms Anderson's theory.

- 64-1762 CANCERIZATION OF A LONG-STANDING CASE OF OSTEOMYELITIS. (Fr.) Foucher, J. (Lyautey Milit. Hosp., Strasbourg, France) and J. Weber. Bull. Soc. Med. Milit. Franc. 56(5): 128-129, 1962.

A case is presented of a 48-year-old man who, 36 yr. after diagnosis of osteomyelitis of the tibia, experienced degeneration of the involved area with involvement of the stroma to form a fibrosarcoma.

- 64-1763 EPIDEMIOLOGIC VIEWPOINTS IN THE INVESTIGATION OF THE ETIOLOGY OF CANCER. (Ger.) Schär, M. (Inst. Soc. Prevent. Med., U. Zürich, Switzerland). Oncologia (Basel) 16(3): 179-185, 1963

The goals and technics of epidemiologic investigation are explained, with examples of the findings of population studies in cancer. Retrospective studies are described, with tables, showing the correlation of cancer incidence with age and occupation; the specific correlation of bronchial carcinoma with the nickel industry in Wales, and the correlation of a high incidence of malignancy in children subjected to frequent prenatal X-irradiation. Prospective epidemiologic studies also are mentioned, their value and their limitations. The technic recommended as most promising for elucidating the cause(s) of cancer, however, is the epidemiologic study of the incidence of malignancy in connection with genetic disorders, such as the frequency of leukemia in mongoloids. However, cancer prevention efforts should be concentrated on environmental carcinogens, which are more amenable to control than genetic factors.

- 64-1764 NEUROBLASTOMA (SYMPATHICOBlastoma) IN NORTHERN IRELAND: A REVIEW OVER A TEN-YEAR PERIOD. (E.) Cochran, W. (Ulster Hosp., Belfast, Northern Ireland). Ulster Med. J. 32(1):82-98, 1963.

A survey was made of neuroblastoma in Northern Ireland. The yearly incidence per million of population determined between 1951-1961 was 2.14 for a total of 30 cases. The comparable incidence in Scotland for 1955-1959 was 2.00. While all deaths from cancer rose from 1.48 to 1.62/1,000 during this period, deaths from neuroblastoma (25) accounted for a little over 0.1%. The 22 deaths in childhood represent 12.5% of all nonleukemic cancer deaths in children. Most of the cases were in children, but there were 2 in the 10-20-yr. age group and 1 woman aged 26. Site of origin, pathologic features, metastatic patterns, and original symptomatology are considered, and found to agree with those reported in prior larger series. Concordant neuroblastoma has been found in identical twins, confuting the impression that presence of the tumor in one may confer immunity to the other. Case histories of 5 survivors are summarized.

- 64-1765 MULTIPLE MELANOMA IN CONGENITAL UNILATERAL LENTIGINOSIS. (Sp.) Amoretti, A. R. (Dr. Manuel Quintela Hosp., Montevideo, Uruguay), R. A. Vignale and E. C. De Vilaboa. Ann. Fac. Med. Montev. 47(5-6):237-245, 1963.

A rare case of segmentary unilateral lentiginosis giving rise to several melanomas, is reported.

- 64-1766 OBSERVATIONS ON CYSTIC MOLES AND CHORION EPITHELIOMAS IN KOREA AND SOUTH CHINA. (Ger.) Huwer, G. (1 Berlin-Tempelhof, Wenckebach St. 23, Germany). Zschr. Geburtsh. Gynaek. 159(3):251-286, 1963.

Among a total of almost 6,000 births in South

China, 38 cases of cystic moles and choriomas were found; among a similar number of births in Korea, 117 such cases were found. The proportion of cystic moles to choriomas was similar in both countries. The tripled incidence in Korea (as compared to South China) may be caused by the increased fertility of the Korean woman. Thus, the av. number of children was, per woman with cystic mole, in Korea 4, in South China 2.5; per woman with cystic mole followed by chorioma, in Korea 5.5, in South China 2.5; per woman who developed chorioma after birth or abortion, in Korea 4.5, in South China 2.5. Other factors which may explain the higher incidence are the prolonged periods of lactation in Korean women and the poor general nutrition with marked protein deficiency which is a result of the Korean diet.

4-1767 AN ANALYSIS BASED ON LOCALIZATIONS, SEX AND AGE GROUPS, REGARDING THE DISTRIBUTION OF CANCER PATIENTS SEEN AT THE ONCOLOGIC INSTITUTE OF BUCHAREST, BETWEEN 1951 AND 1958. (Rum.) Negru, I. (Oncol. Inst., Bucharest, Rumania) and J. Negru. Oncol. si Radiol. 2(1):87-92, 1963.

A statistical analysis of 15,182 subjects with various malignant tumors, percentage distribution according to localization and sex (5756 males and 9426 females) was, resp.: 29.5 (0 and 47.5) uterus; 21.6 (32.9 and 14.6) skin and mucosa; 18 (0.5 and 15.4) breast; 6.3 (9.9 and 4.1) trachea; 6.1 (14.0 and 1.3) pulmonary and pleural; 6.1 (13.2 and 1.8) pharynx and larynx; 3 (9.6 and 2.8) malignant blood diseases; 3.0 (5.5 and 2.1) locomotor apparatus; 2.8 (5.1 and 4) oral cavity; 1.5 (3.9 and 0) male genital organs; 0.7 (0.9 and 0.5) urinary apparatus; 0.6 (0.5 and 0.7) endocrine glands; 0.6 (0.8 and 0.5) nose, sinuses and middle ear; 0.3 (0.5 and 0.1) nervous system; 5.8 (3.6 and 7.2) other localizations (no details). In the same pts., percentage distribution according to age ranges and according to sex (male, female), was: 24, 3.2 (4.9 and 2.1); 25-34, 5.9 (4.5 and 6.8); 35-39, 5.7 (2.9 and 7.4); 40-44, 10.5 (7.0 and 14.6); 45-49, 13.6 (11.4 and 14.9); 50-54, 14.5 (12.2 and 14.0); 55-59, 14.5 (15.9 and 13.7); 60-64, 12.4 (15.2 and 10.8); 65-74, 16.0 (18.8 and 14.3); 75+, 3.6 (4.0 and 3.4) and unknown, 0.3 (0.02 and 0.03).

-1768 RESULTS OF ANIMAL EXPERIMENTS WITH TOBACCO EXTRACTS AND TOBACCO SMOKE CONDENSATES FROM THE VIEWPOINT OF COMPARATIVE HISTOLOGIC ANATOMY. (Ger.) Schmidt, F. (Res. Inst. Exp. Oncol., German Acad. Sci. Pots Dam, Berlin). Deutsch. Gesundheitsw. 18(32):1382-1391, 1963.

Results are reviewed of animal experiments, and the findings of a series of pathologic-anatomic investigations, which indicate an etiologic connection between cigarette smoking and lung

cancer in man. A series of possible measures to be taken are briefly discussed, and a new provision is formulated for insertion in the food labeling law through the German Ministry of Health. This provision would require the labeling of all tobacco products as to the nicotine content of the tobacco. It is also suggested that a general notice of the danger of carcinogenic and cocarcinogenic substances in tobacco smoke, be pointed out on the cigarette packages. In the case of filter cigarettes, a statement would be required as to the proportion of nicotine and tars which is withheld by the filter.

64-1769 RHABDOMYOSARCOMA OF THE ORBIT IN BROTHERS. (E.) Howard, G. M. (Dept. Ophthalmol., Mass. Eye Ear Infir., Boston) and V. G. Casten. Arch. Ophthalmol. (Chicago) 70(3):319-322, 1963.

The occurrence of rhabdomyosarcoma of the orbit is described in 2 of 4 brothers in a family in which there is no other history of malignancy as far back as the grandparents.

64-1770 SOMATIC PECULIARITIES OF PATIENTS WITH CORPUS UTERI CANCER. (Rus.) Bokhman, Ia. V. (Inst. Oncol., Acad. Med. Sci. USSR, Moscow). Vop. Onkol. 9(8):30-37, 1963.

The author gives a short survey of literature concerning the etiology and pathogenesis of corpus uteri carcinoma, describing his own comparative data on the general somatic peculiarities of corpus uteri and cervix uteri cancer pts. An attempt to establish the type of women predisposed to the development of endometrial cancer is made. During prophylactic examination of the population, the author recommends that certain women be distinguished and followed up: those with menstrual disturbances and disturbances of metabolic and generative functions, as well as those suffering from hypertension, chronic hepatitis and fibromyoma of the uterus. A timely treatment of endocrine and metabolic disturbances and precancer will be the best measure for prophylaxis of corpus uteri carcinoma. (Author summary)

64-1771 A HYPOTHESIS REGARDING THE POSSIBLE ROLE OF ANABOLIC STEROID HORMONES AS PROMOTORS OF NEOPLASIA OF BONE AND BONE MARROW AT ADOLESCENCE. (E.) Acheson, R. M. (Dept. Epidemiol., Yale U. Sch. Med., New Haven, Conn.). Yale J. Biol. Med. 36(1):43-52, 1963.

Epidemiological and laboratory studies of normal human growth and of malignant conditions of bone and bone marrow are reviewed. As a result, the hypothesis is put forward that the skeletal and hemopoietic neoplasms of adolescence are a pathological response to the physiological stimulus of the anabolic steroid hormones of puberty. (Author summary)

- 64-1772 ORIGIN OF CARCINOMA OF THE BRONCHUS.
(E.) Dijkstra, B. K. S. (Ubbo Emmius-
singel 73, Groningen, The Netherlands).
J. Nat. Cancer Inst. 31(3):511-519, 1963.

A study of 330 cases of bronchial cancer occurring from January 1, 1950, to January 1, 1960, diagnosed by biopsy, cytology, operation, or autopsy revealed: (1) not every birth yr. contributed equally to the number of cases; (2) the mo. of birth was an important factor, with a high peak late in winter (March). This seasonal influence could be explained by the absence of vitamin A at birth, when the lungs begin to function. Lack of vitamin A at that critical time causes an irreversible metaplasia. Later, this tissue cannot cope with the normal stimuli of life and predisposes the individual to various pulmonary diseases, including cancer. (Author summary)

- 64-1773 THE ORGANIZATION OF ANTI-CANCER SERVICES AND THE FREQUENCY OF CANCER OCCURRENCE IN THE CITY OF BRAILA. (Rum.) Cristescu, M. (Hosp. for Adults No. 1, Braila, Rumania). *Oncol. si Radiol.* 2(3):277-280, 1963.

A brief description regarding hospital facilities available for cancer pts., followed by a statistical study on cancer incidence in the city of Braila (Rumania), during the yr. 1955-1961. The total number of cancer pts. registered in the city + its 3 surrounding districts as compared to the city alone, has increased from 285 and 166 in 1955 to a max. of 422 and 257, resp., in 1961 (minimum of 196 and 108 in 1956). Of the total, 47.3% were males and 52.7% females; 67.1% were older and 32.9% younger than 50 yr.; the ratios of cancer pts./100,000 inhabitants and cancer pts./1000 hospitalized subjects were at a minimum of 148.1 and 12.3, resp., in 1957, a max. of 244.4 and 18.0 in 1958 and were 233.0 and 16.1, in 1961.

- 64-1774 PACHYDERMOPERIOSTOSIS AND CANCER OF THE LUNG. (Fr.) Welfling, J. (Med. Clin., Lariboisiere Hosp., Paris), M. Maitre and P. Bagros. *Rev. Rhum.* 30(6):355-362, 1962.

The authors present the rare case of a combination in the same pt. of an idiopathic pachydermoperiostosis discovered at the age of 20, and a bronchial carcinoma occurring at the age of 45. They recall the principal facts generally known concerning "dysacromélies" and deal with the various hypotheses arising from the case of their pt. (Author summary)

- 64-1775 ON THE GEOGRAPHIC DISPOSITION OF THE CASES OF LEUKEMIA IN THE DISTRICT OF CRACOW. (Pol.) Janicki, K. (3rd Clin. Int. Surg., Cracow, Poland). *Pol. Arch. Med. Wewn.* 33(8): 877-888, 1963.

The geographic disposition of the cases of

leukemia in the District of Cracow has been analyzed. The material consisted of 801 cases of leukemias in pts. living in the District of Cracow, hospitalized in that region and first registered within the yr. 1951 through 1960. The author has concluded that the disposition of leukemia cases was not uniform. The higher incidence of leukemias was related to the localization along the rivers but not along the main roads and railways. The differences in the incidence of leukemias in various counties was statistically significant. The incidence was higher in the northern parts of the District of Cracow. The author believes that the geographic factors as well as the geological, geochemical and geophysical factors play some role in the differentiation of the geographical disposition of the cases of leukemia. (Author summary)

- 64-1776 REGIONAL PECULIARITIES OF CANCER OF THE FEMALE GENITALIA IN THE ADZHARIAN SSR. (Rus.) Charkviani, L. I. (Maternity Hosp., Batumi USSR). *Vop. Onkol.* 9(9):67-73, 1963.

In Adzharia for a 10-yr. period (1952-1961) female genital carcinoma was first diagnosed in 329 cases. On the av., for a year, 28.9 women per 100,000 were ill: vulva and vagina cancer, 0.9; cervix carcinoma, 13.5; corpus uteri cancer, 11.8; adnexa uteri, 2.7. The lowest rate was noted in upper Adzharia (9.8), the highest in Batumi (42.4). Incidence was much greater in Russian women (50.6) than in Georgian and Moslem women (12.9). The ratio of carcinoma of the corpus uteri to cancer of the cervix uteri was 1:1.2, varying from 1:0.2 up to 1:2, depending on the place of residence, profession and nationality of the women. There has been no increase in the rate of incidence of genital cancer; the structure of the morbidity rate changes every 5 yr. Corpus uteri carcinoma occupies the first place in frequency (45.5%). Female genital carcinoma increases up to the age of 50, and decreases after the age of 70.

- 64-1777 FAMILIAL MALIGNANT MELANOMA. A PEDIGREE AND CYTOGENETIC STUDY. (E.) Schoch, E. P., Jr. (3A Med. Arts. Square, Austin, Tex.). *Arch. Derm. (Chicago)* 88(4):445-456, 1963.

Three cases of malignant melanoma occurring in a mother and 2 adult sons in a family of 11 are reported. A study of the pedigree of this family tends to support the generally accepted belief that malignant melanoma is more common in blue-eyed blonds with a light complexion. A cytogenetic study of leukocytes of the mother and one son, in addition to skin cultures of the latter, revealed a normal diploid number of chromosomes (46) and a normal karyotype in the 2 cases.

- 64-1778 PHOTODYNAMIC BIOASSAY OF POLYCYCLIC AIR POLLUTANTS. (E.) Epstein, S. S.

ild. Cancer Res. Found., Boston, Mass.), Small, J. Koplan, N. Mantel, H. L. Falk and Sawicki. Arch. Environ. Health (Chicago) 18(2):531-537, 1963.

teen fractions of organic atmospheric particulates from several American cities were bioassayed for photodynamic activity, and results obtained were expressed as apparent potencies relative to an arbitrary 3,4-benzpyrene (BP) standard (see CRA 1(2):#192 and ibid. (5):#858, 1963). All 6 benzene extracts assayed showed photodynamic activity, with a correlation evident between apparent relative potencies as determined by bioassay, and BP conc. as determined by chemical analysis. Five aliphatic fractions were photochemically inactive. The single aromatic fraction tested had high activity. Three oxygenated fractions showed photodynamic activity, despite absence from them of BP and other polycyclic aromatic hydrocarbons of known structure commonly found in atmospheric particulates. Such oxygenated fractions are reportedly carcinogenic. In reversion experiments, the constituents of neither benzene extracts nor oxygenated fractions interfered with the activity of added BP. Photodynamic bioassay of nine other polycyclic hydrocarbons commonly found in atmospheric particulates showed that their activities and/or atmospheric conc., generally, were so limited as not to contribute materially to the potencies of the samples. (Author summary)

779 EPIDEMIOLOGY OF LUNG CANCER AND 3,4-BENZPYRENE IN PRAGUE ATMOSPHERE. (E.) Smolenský, V. (2nd Dept. Med. Chem., Charles U., Prague). Neoplasma (Bratisl.) 10(4):413-418, 1963.

In the urban population in Czech and Moravia was divided into 3 groups (towns with over 1,000,000, 100,000 or over 50,000 inhabitants), primary carcinoma of the lung in the male was statistically elevated only in the first group (Prague). Elevation of male mortality in cancer of the lung in Prague is in a harmony with the higher levels of 3,4-benzpyrene in Prague's atmosphere, especially in the winter season (see CRA 1(7):#17, 1963).

780 AN AUTOPSY CASE OF AN ATOM BOMB SURVIVOR WITH LEUKEMIA. (Jap., Abstract) Ito, Y. (Osaka Red Cross Hosp., Japan) and Oshizaki. Rinsho Ketsueki (Jap. J. Clin. Lab.) 4(2):203, 1963.

In discussion following presentation of the case, Ito, Y. stated that according to a statistical study at Nagasaki, the incidence of leukemia was significantly higher in people who have been exposed within 2000 meters of the atom bomb hypocenter; there is no difference between unexposed people and people who have been exposed at more than 2000 meters from the center. Hence he believes that the case reported, who was 4.5 Km from the center, was not related to exposure to the bomb.

64-1781 LEUKEMIA CLUSTER IN NILES, ILL. IMMUNOLOGIC DATA ON FAMILIES OF LEUKEMIC PATIENTS AND OTHERS. (E.) Schwartz, S. O. (Hektoen Inst. Med. Res., Cook County Hosp., Chicago), I. Greenspan and E. R. Brown. J.A.M.A. 186(2):106-108, 1963.

Eight cases of childhood leukemia were diagnosed in a small community (see CRA 1(5):#978, 1963). Blood was obtained from members of these and four other leukemic patients' families. The sera were tested for antibodies to leukemic antigens. Antibodies were present in 1-3 members of every family. Positive reactors most often were the mother or a sibling closest in age to the patient with leukemia. Antibodies were not found in control sera or in patients with leukemia. We interpret these findings to mean that exposure to leukemogenic viruses leads to the formation of antibodies in some and leukemia in others. Not all those who fail to develop demonstrable antibodies develop leukemia, which suggests that present techniques of demonstrating the antibodies may be inadequate. The absence of antibodies in patients with leukemia is, on the other hand, thought to be part of the disease syndrome. (Author summary)

64-1782 SEASONAL VARIATION IN LEUKAEMIA INCIDENCE. (E.) Lee, J. A. H. (London Hosp. Res. Lab., E.1). Brit. Med. J. 1:623, 1963.

As previously reported, in the age range 0-19 years there is a summer peak in the incidence of the onset of clinical acute lymphatic leukemia reported under the National Cancer Registration Scheme. The same has now been found to be the case for adults 20-44. There is no clear seasonal variation in the onset of acute myeloid and monocytic leukemia.

64-1783 LYMPHOMA. A GEOGRAPHICAL STUDY OF LEUKEMIA AND LYMPHOMA IN KANSAS, 1950-1959. (E.) Martin, D. C. (Dept. Microbiol. Med., U. Kansas Med. Ctr., Kansas City), A. A. Werder, W. E. Larsen, T. D. Y. Chin and A. Roth. J. Kansas Med. Soc. 64(11):477-486, 1963.

A 10-yr. study of leukemia and related neoplasms in Kansas was carried out utilizing 2,740 cases. The following observations are made: (1) There is some grouping of counties with high incidence, but not sufficiently to make an obvious explanation for the localization. (2) The proportion of the population in older age groups is an important factor in explaining the variation in death rates among counties and regions. (3) The death rate for leukemia et al. is significantly higher in urban areas than in rural areas. (4) The highest death rate is in small towns (2,500-5,000) and the death rate declines as the population of the urban areas increases. (5) With age adjustment the death rates of leukemia and lymphoma in small towns approximate those in the cities with larger population. (Author summary)

64-1784 MELANOMA. A TEN-YEAR RETROSPECTIVE SURVEY IN NEW ZEALAND. (E.) Watson, E. C.

Aust. New Zeal. J. Surg. 33(1):31-46, 1963.

Reported are all 666 hospital cases registered with the Medical Statistical Dept. from January 1949 to December 1958. Ratio of male:female was 5:8; alive and well, 5:13; dead, 6:5; the av. age of living pts. was 46 yr. and at time of death 50.7 yr. The principal sites of occurrence were: head and neck 190 cases (30%), leg 163 (24.5%), trunk 99 (15%); these figures closely parallel American findings (Gordon, 1953). While the normal proportion of Maori to European is 1:12, the actual incidence of melanoma was lower, 8 and 635, resp.; in 31 cases race was unknown.

64-1785 CANCER AND OCCUPATION. STATISTICAL INVESTIGATION OF STOMACH AND LUNG CARCINOMA. (Ger.) Berndt, H. (Robert-Rossle Clin., German Acad. Sci., Berlin). Krebsarzt 18(7/8):289-296, 1963.

A statistical comparison of the distribution of professions in 1,724 male pts. with lung cancer and 406 men with stomach cancer yields significant differences. In pts. with carcinoma of the bronchus the frequency of the following professions is significantly greater: metal workers, especially turners, mechanics, mounters, also woodworkers and those in commercial occupations. The following professions are significantly more frequent in pts. with carcinoma of the stomach than in men with lung cancer: building workers, iron forgers, occupations in the world of arts and those in intellectual fields, and those in legal and administrative activities. Partially these results are in accordance with our conceptions concerning the etiology of these tumors, but in part there is no convincing interpretation of the observations. (Author summary)

64-1786 CANCER OF THE STOMACH IN PUERTO RICO: TEN YEARS DISTRIBUTION 1950-1959. (E.) Martinez Martinez, I. (Centl. Cancer Registry, Dept. Health, Santurce, Puerto Rico). Bol. Asoc. Med. P. Rico 55(1):12-32, 1963.

Cancer of the stomach has accounted for the greatest number of deaths from cancer in Puerto Rico during the ten years of the study. Illness and deaths from cancer of the stomach increased with age. The male group in almost all age groups had the greatest incidence and mortality rates. The over all male-female incidence and mortality ratios was two to one. The microscopically confirmed cases were more frequent in the Northeast Health District which had the best diagnostic and treatment facilities on the Island. The deaths from cancer of the stomach during the years 1956 to 1959 occurred in greater numbers among agricultural workers, laborers, and private household workers. Puerto Rico held an intermediate rank in mortality rate from cancer of the stomach among 23 different countries. The stomach cancer mortality rate on the Island

was almost 3 times higher than the rate for the white population of the United States, but is half the rate for Japan. Incidence and mortality trends from cancer of the stomach in Puerto Rico were stable, showing perhaps the beginning of a decrease.

64-1787 CANCER EPIDEMIOLOGY. (Sp.) Martinez Martinez, I. (Centl. Cancer Registry, Dept. Health, Santurce, Puerto Rico). Bol. Asoc. Med. P. Rico 55(8):321-337, 1963.

Statistics from Puerto Rico (1950-1961) gave the following mortality rates/100,000 for males (10,738 cases): stomach, 22.8; esophagus, 8.0; bronchus + trachea + lung, 6.4; prostate, 4.9; leukemia + aleukemia, 3.1; liver, 2.9; larynx, 2.9; large intestine (except for rectum), 2.5; urinary organs, 2.4; pharynx, 2.3; others, 20.0. In 9,036 females rates were: uterus, 16.5; stomach, 11.4; breast, 4.2; esophagus, 3.4; large intestine (except for rectum), 3.0; liver, 2.7; leukemia + aleukemia, 2.6; bronchus + trachea + lung, 2.3; pancreas, 1.6; all others, 16.8. Over the 12-yr. period, the age-adjusted mortality for males increased from 105 to 140/100,000, whereas that for females remained at about 108/100,000. Significant increases have been observed in deaths from digestive, respiratory and esophageal cancer in men, and for leukemia + aleukemia in both sexes. In women, mortality from cancer of the reproductive organs has dropped significantly.

64-1788 PRIMARY CHOLECYSTIC CARCINOMA: A VANISHING ENTITY. (E.) Barbosa, E. (Campinas, Sao Paulo, Brazil) and R. G. Rate. J. Int. Coll. Surg. 40(5):429-432, 1963.

The incidence of primary carcinoma of the gall-bladder is discussed, and its progressive decline in the American literature over the past 60 years is cited. In the author's opinion, primary cholecystic carcinoma is a vanishing entity, since cholecystectomy is being performed more routinely for benign disease and serves "prophylactically" against malignant change. (Author summary)

64-1789 SIGNIFICANCE OF URINARY RETENTION IN THE ORIGIN OF BLADDER TUMORS. (Ger.) Perelman, W. M. (Centl. Inst. Postgrad. Med. Educat., Moscow) and A. L. Schabad. Zschr. Urol. 56(8/9):473-478, 1963.

Cancer of the urinary bladder attacks men more frequently than women. This circumstance can be associated with the occurrence of urinary retention in older men. Among the 167 bladder cancer pts. investigated by the author at the urological department of the Botkin Hospital (140 men and 27 women), voiding disturbances were ascertained in 92 men (adenomas of the bladder neck, prostate stones, bladder stones, and bladder diverticuli).

us, 65.7% of the men who became ill with cancer of the urinary bladder had a bladder voiding disturbance to a slighter or more severe degree. The impression is formed, that urinary stasis provides additional favorable conditions for the origin and development of a urinary bladder tumor. The removal of obstructions in the region of the bladder neck is a necessary prophylactic measure against tumor formation in the bladder against its recurrence. (Author summary)

1790 FAMILIAL LEUKEMIA: REPORT OF INSTANCE AND REVIEW OF THE LITERATURE. (E.) Meier, K. H. (Mayo Clin., Rochester, Minn.) and E. D. Bayrd. Proc. Mayo Clin. 38(24):531, 1963.

The familial occurrence of acute myeloid leukemia is reported in a boy aged 5 and his mother; a brief review of the literature (38 references) is presented. These 2 pts. (and no other members of the family) were exposed, simultaneously and intensely, to inhalation of and contact with insecticide 8 mo. and 4.5 yr., resp., prior to the onset of leukemia.

1791 FAMILIAL OCCURRENCE OF LETTERER-SIWE DISEASE. (E.) Schoeck, V. W. (Variety Club Heart Hosp., U. Minnesota, Minneapolis), D. A. Peterson and R. A. Good. Pediatrics 66(6):1055-1063, 1963.

The authors describe the occurrence of Letterer-Siwe disease in 2 brothers (one born 10 mo. after the death of the other) who were diagnosed at the ages of 7 mo. and 7 wk. A review of the literature on other familial occurrences is presented. The 2 children reported were born in 2 different environments (Venezuela and Minnesota).

1792 AN EXTRA ABNORMAL CHROMOSOME IN A CHILD WITH MONGOLISM AND ACUTE MYELOBLASTIC LEUKEMIA. REPORT OF A CASE. (E.) Kruger, R. D. (Dept. Pediat., Cleveland Clin., Cleveland), M. K. Keller and D. Lonsdale. Cleveland Clin. Quart. 30(4):215-224, 1963.

A case is reported of a 16-month-old Negro girl with mongolism and acute myeloblastic leukemia in the cells of whom there were 2 chromosome populations. One group contained 48 chromosomes with an extra chromosome in group C(6-12) and somy-21; the second group contained 47 chromosomes with only trisomy-21.

1793 BENZENE EXPOSURE AND APLASTIC ANEMIA FOLLOWED BY LEUKEMIA 15 YEARS LATER.

(E.) De Gowin, R. L. (Dept. Med., U. Chicago Med. Sch.). J.A.M.A. 185(10):748-751, 1963.

A case is presented of a painter who had been exposed to benzene for 13 yr. and who after 15 yr. presented the hematological picture characteristic of acute myeloid leukemia.

64-1794 EXPERT OPINION ON THE RELATION BETWEEN PULMONARY TUBERCULOSIS AND LUNG CANCER. (Ger.) Schüttmann, W. (Germ. Cent. Inst. Social Med., Berlin-Lichtenberg). Deutsch. Gesundh. 18(25):1077-1084, 1963.

A case is presented of a lung resection for bronchial carcinoma. Since some tuberculous changes were found in the specimen, an attempt was made to associate this with possible occupational exposure to tuberculosis (in a dairy) 22-35 yr. before diagnosis. This association was denied. On appeal the original ruling was again supported. The literature on the possible causal relationship between tuberculosis and lung cancer is reviewed (48 references).

64-1795 DO SURFACE ACTIVE SUBSTANCES HAVE A RELATIONSHIP TO LEUKEMIC MANIFESTATIONS? (Cz.) Preis, A. (Purkyne U., Brno, Czech.), B. Polák, B. Pohl and J. Nováková. Cas. Lek. Cesk. 102(24):677-679, 1963.

A case is presented of a 3-year-old girl who accidentally ingested some saponated cleaning fluid and who later developed leukemia.

64-1796 MULTIPLE MALIGNANT PRIMARY TUMORS OF THE ORAL CAVITY AND THE UPPER RESPIRATORY TRACT. (Ger.) Kuhn, E. (Cancer Radiol. Inst., Gen. Hosp., Budapest, Hungary). Zschr. Laryng. Rhinol. Otol. 42(7):521-528, 1963.

During a period of 14 yr., among those treated, a total of 36 pts. (30 male, 6 female, age 42-79 yr.) had multiple malignant primary tumors of the oral cavity and the upper respiratory tract. Histologically the tumors were squamous cell carcinomas; they were synchronous (within 6 mo.) in 12/36 (33.3%), and metachronous in 24. Family history was positive in 30, among whom 8 had cancer; 85% of the pts. were smokers. Among 33 pts. studied, leukoplakia was present in 21 and was most severe in those cases with more than 2 tumors; 9/36 had a history of syphilis and 6/9 exhibited syphilitic leukokeratosis. Among the metachronous cases, the intervals varied from 1 to 27 yr. In cases where the precancerous changes were severe, the latent period for the second tumor was briefer.

MISCELLANEOUS

- 64-1797 EXPERIMENTAL STUDIES OF FACTORS INFLUENCING THE DEVELOPMENT OF HEPATIC METASTASES. XIII. EFFECT OF HEPATIC TRAUMA IN PARABIOTIC PAIRS. (E.) Fisher, E. R. (Dept. Path., U. Pittsburgh, Pa.) and B. Fisher. Cancer Res. 23(6):896-900, 1963.

The incidence and size of hepatic metastases in parabionts subjected to intraportal inj. of Walker tumor cells were similar to those observed in single animals receiving comparable numbers of tumor cells regardless of whether the liver of the contralateral member was manipulated or not. Similarly, no enhancing or other effect on these hepatic tumors was encountered when partial hepatectomy was performed in the uninjected parabiont. On the other hand, metastases were found only in the livers of those uninjected parabionts subjected to hepatic manipulation. A few animals subjected to partial hepatectomy also exhibited hepatic metastases when partial hepatectomy was performed immediately after tumor cell inj. in the contralateral member. This effect of manipulation was noted when parabiotic pairs were separated as early as 20 min. after tumor cell inj., although the incidence and size of lesions in the manipulated livers were not as great as those noted when separation was performed at 3 days or 2 wk. The incidence and size of pulmonary metastases were comparable in both parabiotic members in all instances. Manipulation of spleen or kidney failed to influence the incidence of metastases within these organs or the liver. (See also CRA 1(5):#795, 1963.) (Author summary)

- 64-1798 INVESTIGATIONS CONCERNING THE ROLE OF A HUMORAL FACTOR IN LIVER REGENERATION. (E.) Fisher, B. (Dept. Surg., U. Pittsburgh Sch. Med., Pa.), E. R. Fisher and E. Saffer. Cancer Res. 23(6):914-920, 1963.

In an effort to obtain evidence for or against the existence of a humoral factor controlling hepatic regeneration, observations in over 800 rats have resulted in the following: (a) Plasma obtained from hepatectomized donors inj. into normal rats either i.v. or i.p. resulted in an increase in mitoses of similar magnitude to that observed when plasma from normal donor rats was inj. No significant increase in hepatic DNA synthesis as determined by incorporation of P^{32} into DNA resulted when either route of admin. was employed. (b) Serum obtained from hepatectomized normal and cirrhotic rats and inj. i.v. or i.p. failed to significantly increase mitoses. DNA-phosphorus specific activity was no greater than that observed following the inj. of normal serum. (c) With a variety of time relationships between hepatectomy, P^{32} inj. and sacrifice of animals, no definite evidence of increased DNA synthesis in the intact normal member of a parabiotic pair occurred following hepatectomy in the other which was either normal or cirrhotic.

Likewise, no effect upon mitoses in the intact member was observed. Following sham operation in parabiotic rats an increase in mitoses was not seen. The great variation in the number of mitoses encountered in all experiments performed tends to minimize the value of this parameter as an index of hepatic parenchymal response to a specific factor. (Author summary)

- 64-1799 STUDY OF THE EFFECT OF *SERRATIA MARCESCENS* AND *STREPTOCOCCUS PYOGENES* ON THE TRANSPLANTED OSTEOGENIC SARCOMA IN WISTAR RATS. (Jap.) Yukawa, Y. (Dept. Orthoped., Tokyo Med. Dent. Coll.). Ochanomizu Igaku Zasshi (Ochanomizu Med. J.) 11(1):1-23, 1963.

Young Wistar rats (av. wt. 80 g) after 3 monthly doses of P^{32} (1 μ C/g), were given a single inj. of crystalline 3,4-benzpyrene (15 mg) into the bone marrow of the tibia. Further P^{32} was administered for approx. 10 mo. (total dose 2.1 mC, i.p.) until osteogenic sarcoma or fibrosarcoma was produced in the metaphyses of the tibia. Some of the tumor material was transplanted s.c. into the trunk of other young rats and the resultant tumor tissue was used in a culture medium for growing the 2 species of bacteria, alone and together. The effects of both toxin and cell suspensions of these bacteria were tested on the original tumor transplanted into mice. The toxin resulted in slight prolongation of survival time of the mice as did the cells, but the cells also suppressed tumor growth. Both produced degenerative changes of tumor tissues.

- 64-1800 COMPLETE INHIBITION OF OCCURRENCE OF SPONTANEOUS HEPATOMAS IN HIGHLY SUSCEPTIBLE (C3H x YBR) F_1 MALE MICE BY HYPOPHYSECTOMY. (E.) Heston, W. E. (NCI, Bethesda). J. Nat. Cancer Inst. 31(2):467-474, 1963.

No hepatomas occurred in genetically highly susceptible $A^Y A$ and Aa male (C3H x YBR) F_1 hybrid mice hypophysectomized at 6 wk. of age and maintained to the advanced age of 16 mo. Hepatomas were found in 100% of the intact control $A^Y A$ male hybrids of the same age, with an av. of 5.6 hepatomas per animal, and in 88% of the intact control Aa male hybrids of the same age, with an av. of 3 hepatomas per animal. The greater occurrence of hepatomas in the $A^Y A$ than in the Aa controls confirms the previous observation that the A^Y gene increases the occurrence of spontaneous hepatomas (Author summary)

- 64-1801 QUANTITATIVE RELATIONSHIPS IN TUMOURS INDUCED BY A VIRUS, AND BY OTHER AGENTS. (E.) Blum, H. F. (NCI, Bethesda). Nature (London) 199:155-156, 1963.

A reevaluation of Bryan's relationship between

s dose and between admin. and tumor appearance made from data obtained with the use of Rous oma, taking into account cell division of the late carrying the information determining the rate of cell division (assumed to include al template). New proportionality constants been defined: an assumed proportionality een rates of virus and cell proliferation, and orptionality between dose and number of virus icles. The model appears to fit data for genic, but not for other viruses or for viru- bacteriophage infections. The new mathe- cal relationship is also compared to models umor induction by UV light and by chemical ts. A consideration of the quantitative re- onships indicates that the mechanisms for three types of carcinogenesis are very dif- nt, suggesting that current theories attrib- all neoplasms to viruses are not tenable. ver, a common denominator for all types of lasms should be searched for at the level of rmation transferral in the proliferating er cell.

802 A RADIOAUTOGRAPHIC ANALYSIS OF CELLULAR PROLIFERATION IN DYSPLASIA AND CARCINOMA *IN SITU* OF THE UTERINE CERVIX. (E.) Richart, J. (Coll. Physicians Surg., Columbia U., New York). *Am. J. Obstet. Gynec.* 86(7):925-930, 1963.

izing radioautographic analysis, it was deter- d that the stages in the development of car- ma *in situ* in the human uterine cervix are anied by altered labeling indices (labeled ei/total number of nuclei) that increase rithmically with severity. There is a grad- replacement of the layers of epithelium, nor- y composed of cells in a mitotic end stage, ells that retain the ability to produce hter cells. Not only is there an increase he number of cells capable of division, but e is an increase in the rate at which these s divide. In carcinoma *in situ* the population ars to be essentially homogeneous in terms of labeling index. (Author summary)

803 INTRAVENOUS INJECTION OF GUERIN EPITHELIOMA SUSPENSION. V. IN THE RAT AFTER BLOCKING OF THE RETICULOENDO- CIAL SYSTEM WITH TRYPAN BLUE. (Fr.) ssens, J. (Cancer Res. Inst., Lille, France), anlerenberghe, A. Clay, L. Adenis and uandalle. *C. R. Soc. Biol. (Paris)* 157(3): 560, 1963.

skade of the RES of the Wistar rat with trypan e results in a significantly greater spread eans of the blood stream of Guérin epithelioma ensions. This increase is of the same order hat obtained after splenectomy and shows the e characteristics.

64-1804 PARABIOSIS AND WALKER CARCINOSARCOMA. (It.) Levi, A. (Inst. Pharm., U. Modena, Italy). *J. Urol.* 90(2):169-171, 1963.

In Sprague-Dawley rats resection of transplanted Walker carcinosarcoma (s.c.) caused immunologic resistance to further tumor inoc. lasting for at least 6 mo. Treatment of rats by s.c. inj. with serum (0.2 ml) or blood (0.25 ml) taken from rats with actively growing tumor every 10 days for 2 mo. (6 inj.) prior to tumor inoc. did not prevent tumor take, but on continued treatment regression of all tumors was seen in treated animals at about 2 mo. after inoc. Similarly, inj. of serum or blood from the time of tumor inoc. caused tumor regressions beginning at about 2 mo. later (com- plete after 12 inj.). Rats with regressed tumors were resistant to further tumor inoc. In 10 pairs of parabiotic rats attempts at inoc. of a second parabiont were consistently unsuccessful for up to 4 mo. once the first rat had a well developed tumor. In 2 more pairs of parabionts tumors did not take on first inoc., and in these cases attempts at inoc. of the second parabiont were also consistently unsuccessful.

64-1805 DIFFERENTIAL BEHAVIOUR OF TRANSPLANTED MOUSE LYMPHOMA LINES IN GENETICALLY COMPATIBLE HOMOZYGOUS AND F₁ HYBRID MICE. (E.) Hellström, K. E. (Inst. Tumor Biol., Karolinska Inst. Med. Sch., Stockholm). *Nature (London)* 199:614-615, 1963.

Variant sublines of a lymphoma LNSF originally from an A/Sn x A.SW F₁ hybrid (2 isogenic resis- tant mouse strains differing at the histocompati- bility-2 locus) were obtained with irreversible loss of the histocompatibility-2 antigens specific for A (4 variants), and for A.SW (2 variants). On comparison of the variants with the unselected F₁ tumor from which they were derived for ability to grow in mice of the original F₁ genotype it was found that the variants grew less well in the F₁ hybrids than the unselected lines. Mechanism of the phenomenon remains to be clarified, al- though two alternatives appear possible, one based on a graft-versus-host reaction, the other on a host-versus-graft response. The results also suggest that cells with certain antigens may be selected from large populations of cells lack- ing these antigens, and experiments of this type are in progress.

64-1806 THE STUDY OF TOLERANCE AND OF THE POTENTIATION PHENOMENON IN RELATION TO THE BROWN-PEARCE CARCINOMA OF RABBITS. (E.) Radzikhovskaya, R. M. (Inst. Exp. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). *Biull. Eksp. Biol. Med. (Eng.)* 53(6):667-669, 1963.

Pretreatment (i.p. or s.c.) of adult rats with frozen extracts of Brown-Pearce carcinoma from rabbits failed to stimulate tumor growth on

subsequent tumor inoc. 14-21 days later. Of 60 rats receiving preliminary treatment, only 3 developed tumors, all subsequently reabsorbed. None of 40 control rats developed tumors, confirming the natural species resistance of rats to the tumor heterotransplants. However, pre-inoculation of Brown-Pearce tumor frozen extracts or of normal rabbit organ extracts into newborn rats followed by tumor transplant at 5-6 days after birth gave 100% tumor takes. Deaths from tumor were 26/40 and 17/25, resp.; in the remainder the tumors were resorbed. Controls showed tumor takes and deaths from tumor in only 6/30 and 1/30, resp. The results indicate for the Brown-Pearce carcinoma that tumor tolerance and tumor potentiation are different immunologic processes, either due to different antigens or to differences in conditions required for the expression of a common antigen.

- 64-1807 NUCLEAR RIBOSOMES, MESSENGER-RNA AND PROTEIN SYNTHESIS. (E.) Allfrey, V. G. (Rockefeller Inst., New York). Exp. Cell Res. Suppl. 9:183-212, 1963.

Particles of ribonucleoprotein ("ribosomes") are generally recognized to be the main sites of protein synthesis in the cytoplasm of both normal and malignant mammalian cells, and in plant cells, fungi, yeasts, and many bacteria. Evidence is presented to show that ribosomes also occur within cell nuclei, that they play a major role in the synthesis of nuclear proteins and that their continuing function depends on the synthesis of "messenger"-type RNA. Some methods for the isolation of thymus nuclear ribosomes are described, together with analytical data on their chemical composition and physical properties.

- 64-1808 CHANGES IN TRANSPLANTED CELLS AND IN CELLS CARRIED ON LABORATORY MEDIA FOR SOME TIME. (Dut.) Bruyn, W. M. de (Dept. Exp. Cytol., Antoni van Leeuwenhoek Inst., Amsterdam). Nederl. T. Tandheelk. 107(36):1614-1619, 1963.

An attempt has been made to explain why transplanted cells, as well as cultured cells derived from normal tissue, may after some time begin to grow uncontrollably. After explantation, the cell's control systems, which are adapted to the effect of its own "microclimate", are no longer used, and become inactive. When implanted in an isologous host the cells, no longer "responsive" to the control system of their host, continue to grow and produce a tumor. This inactivation might be a phenomenon similar to that of the "loss" of certain structures, functions and antigens in cells which have been carried on laboratory media for some time. The many factors which may affect the successful grafting of cells cultured in vitro and then implanted in an isologous host are discussed. Although it is difficult to explain the apparently contradictory results obtained by different workers (the "loss" of tumor

producing capacity and the "malignant transformation" of cells in tissue cultures), some factors which may have been of importance are mentioned. (Author summary)

- 64-1809 LEUKEMIC AFFECTIONS IN CHICKENS WITH POSITIVE TUBERCULIN TESTS. (Rus.) Mukhamedshin, R. A. (Leningrad Veter. Inst., RSFSR). Vop. Onkol. 9(8):80-83, 1963.

The internal organs of chicks with positive tuberculin reaction were examined for the possibility of leukemia. In 130-day-old chicks, 103/188 livers, 120/184 spleens, 27/152 kidneys, 17/162 hearts, 37/103 ovaries, 42/118 lungs had leukemic changes. The figures for 150-day-old chicks were, resp., 58/98, 66/97, 40/69, 9/59, 36/61, and 31/54. In the first group 136/197 had definite, and 9/197 suspected, leukemic changes. In the second group these figures were, resp., 46/193 and 29/193.

- 64-1810 CONTRIBUTIONS TO THE STUDY OF ANTITUMOR IMMUNITY. (Rum.) Baroni, V. (Inst. Endocrin., Bucharest, Rumania) and H. Zimel. Oncol. si Radiol. 2(1):45-51, 1963.

Homologous testicular tissue, which is rich in hyaluronidase, when implanted into Wistar rats before transplantation of Walker 256 adenocarcinoma, resulted in tumor inhibition in 10/20, probably by producing hyaluronidase antibodies in the body. When testicular tissue was implanted concomitantly with implantation of the adenocarcinoma, there was no significant effect on tumor development. In parallel experiments, in 2 groups of rats given transplants of calf thymus tissue (which is deficient in hyaluronidase) there was no decrease in the rate of tumor development; on the contrary, there was slight stimulation of tumor growth.

- 64-1811 HISTOCHEMICAL STUDY OF CERTAIN OXIDIZING ENZYMES DURING SPONTANEOUS MALIGNANT TRANSFORMATION OF FIBROBLASTS IN TISSUE CULTURES. (E.) Raikhlin, N. T. (Inst. Exp. Clin. Oncol., USSR Acad. Med. Sci., Moscow) and N. S. Staroverov. Fed. Proc. 22(3):T576-T581, 1963.

With the object of studying the principles governing the energy metabolism of cells during prolonged cultivation and in the course of spontaneous malignant transformation, several oxidation-reduction enzymes were investigated histochemically by means of nitro-blue tetrazolium (nitro-BT). Analysis of the results shows that the activity of succinate-nitro-BT-reductase, DPN-, and TPN-nitro-BT-reductase and cytochrome oxidase varies in fibroblasts in different stages of monolayer cultivation. Three principal stages can be observed. The first stage includes the first days of cultivation, when the activity of the succinic dehydrogenase and the diaphorases, followed by that of cytochrome

case, falls sharply in the cells deprived of usual conditions of existence. In this period disturbance of the physical state of the mitochondria is observed, as shown by the marked polymorphism of the intramitochondrial deposits of amazan. The second stage (from 15-30 days to 60 mo.) is characterized by high enzymic activity in the majority of cells, but at this period cells with moderate or weak activity may also be encountered. The third stage (from 7-10 mo. and after), coinciding with the onset of malignant transformation of the cells (Staroverova, and others), is characterized by a new decrease in the activity of succinic dehydrogenase, cytochrome oxidase and, to a lesser degree, N- and TPN- diaphorases in most cells. In the first stage, the decrease in the enzymic activity of the connective tissue cells is temporary, cells soon regain their high activity. In the third stage, the decrease in the activity of oxidation-reduction enzymes studied is more long and possibly irreversible. This suggests that different mechanisms are responsible for the changing of activity in the early and late stages. (Author summary)

12 MAMMARY TUMORS, MAMMARY GLAND DEVELOPMENT, AND MORPHOLOGY OF OVARIES IN MICE OF STRAINS C3H, CBA AND THEIR F₁ HYBRIDS. (E.) Richardson, F. L. (Roscoe B. Jackson Mem. Lab., Bar Harbor, Maine) and J. L. J. Nat. Cancer Inst. 31(3):529-539, 1963.

Comparison of the rate of tumor development in female mice of high-mammary-tumor strains C3H and CBA/J and their F₁ hybrids showed a significant difference between the av. tumor age of the hybrid with the C3H mother and the hybrid with the CBA mother. The reciprocal hybrids had tumors at mean ages closely approximating those of the maternal parent. This indicated that the agent in the milk of C3H females was stimulating to early development of mammary tumors more than that in the milk of CBA mice. The incidence of tumors was high in all groups. All mammary glands were similar in degree of lateral branching or acinar proliferation. Microscopic sections of the ovaries of all groups were alike in structure except that in old CBA females the ovaries usually showed infiltration of amyloid. Corpora lutea and follicles were present and persisted for most of the lifetime of the mice. Thus there seems to be a correlation between the quantity of hormone-producing components of the ovaries, morphology of the mammary glands, and incidence of mammary tumors in virgin mice of high-mammary-tumor strains. (Author summary)

13 TRANSPLANTED TUMOR GROWTH AND LIVER REGENERATION IN THE RAT. (E.) Gershbein, M. A. (Dept. Biol., Ill. Inst. Tech., Chicago). Cancer Inst. 31(3):521-528, 1963.

Subcutaneous transplantation of Walker 256 and Flexner-Jobling carcinomas or the Jensen sarcoma into young adult male rats at, or 5 days before, partial hepatectomy did not significantly alter the extent of liver regeneration over a period of 10.5 days. When the Walker or Jensen tumor cells were inj. into the caudal or either of the caudate lobes, hepatic regeneration was not affected, but tumor growth was markedly accelerated in the partially hepatectomized rats, except for 1 series of old animals. When partial hepatectomy was carried out 72-96 hr. after transplantation of Walker tumor cells or fragments in the caudal lobe, the lesion weights were in the control range at necropsy performed on the 7th or 8th day. However, no statistically significant increase in tumor growth rate occurred where the lesion was transplanted s.c. in animals killed over intervals up to 16 days. The hepatic water content increased in partially hepatectomized rats but was not further elevated by the presence of tumor either subcutaneously or in the liver. (Author summary)

64-1814 THE EFFECT OF GIBBERELIC ACID ON MAMMALIAN (XC TUMOUR) CELLS IN TISSUE CULTURE. (E.) Chýle, P. (Inst. Exp. Biol. Genet., Czech. Acad. Sci., Prague). Folia Biol. (Praha) 9(4):312-313, 1963.

It is generally held that animal cells are not responsive to the gibberellins. Nevertheless long term cultivation of rat sarcoma XC was facilitated by a 5 mg% supplement of gibberellic acid to the culture fluid. (Author summary)

64-1815 OCCURRENCE OF HAEMOGLOBIN H IN LEUKAEMIA. (E.) Beaven, G. H. (Med. Res. Council Lab., London, N.W. 3), B. L. Stevens, N. Dance and J. C. White. Nature (London) 199:1297-1298, 1963.

Among previously described adult cases of erythro-leukemia, 3 were exceptional in showing red cell inclusion bodies after supravital staining, associated with the presence of a minor hemoglobin component with electrophoretic properties very similar to those of H-H (Hb- β_A^H). A case is described of atypical chronic myeloid leukemia in a 56-year-old male of known British descent which exhibits similar red cell inclusion bodies, associated with the presence of about 10% of a minor hemoglobin, with no detectable proportions of Hb-F and Hb-Bart's (Hb- γ_4^H) and no alteration in the level of the normal minor hemoglobin. The abnormal hemoglobin has now been identified as Hb-H.

64-1816 THE INFLUENCE OF ELECTRICAL STIMULATION OF THE HYPOTHALAMUS UPON THE DEVELOPMENT OF EXPERIMENTAL OVARIAN TUMORS. (Rus.) Ukolova, M. A. (Rostov Inst. Radiol. Oncol., USSR) and Yu. N. Bordiushkov. Vop. Onkol. 9(10):40-43, 1963.

A prolonged repeated electrical stimulation of the rat hypothalamus provoked an inhibition of growth and complete resolution of intrasplenic ovary transplants during early stages of development. The testing of the hypophysis tissue of the experimental animals showed this influence was not connected with decrease of gonadotropic hypophyseal activity. The electric stimulation of the hypothalamus of rats with ovary tumors developing out of the transplants did not provoke any inhibition of the tumorous growth but stimulated it. (Author summary)

64-1817 BACTERIAL CARCINOGENS. (E., Abstract)
Brandt, J. W. Excerpta Med. (Internatl. Cong. Ser. 62) (4):E91, 1963.

A group of workers at the NIH have isolated from a variety of human and animal tumors a pleomorphic organism which in one phase of its life cycle is filterable and thus resembles a virus. When placed on a special medium, the organism grew to a bacillus. When inj. into animals which are nearly immune to cancer, such as guinea pigs and certain strains of rats, a variety of cancerous tumors developed, some of which metastasized. The organism has been obtained from the tumors. Using the organism to prepare a vaccine, an antibody of high agglutinating titer was developed.

64-1818 THE EFFECT OF CROCKER SARCOMA GROWN ON CHORIOALLANTOIC MEMBRANE UPON THE GROWTH OF CHICK EMBRYO. (Rus.) Maevskaia, T. M. (Ivanovskii Inst. Virol., Acad. Med. Sci. USSR, Moscow) and R. M. Mukhina. Vop. Onkol. 9(11): 12-15, 1963.

Mouse Crocker sarcoma was adapted to the chorio-allantoic membrane of the chicken embryo and passed 400 times, without changing its basic properties. During prolonged passage any tumor toxicity for the developing chicken embryo was found to be absent. The wt. of chicken embryos and their organs as well as their blood hemoglobin contents were normal. Tumorous cells of the Crocker sarcoma cultivated on a chorioallantoic membrane get into the blood of the chicken embryos which is determined when blood is inoc. into mice. The inoc. of chicken embryo organs fails to provoke any tumor development in mice, while after inoc. with the sarcoma, the organs of hatched chicks not more than 7 days old did induce neoplasms in mice. (Author summary)

64-1819 STUDIES ON THE IMMUNITY TO HUMAN SARCOMA. (Rus.) Malysheva, S. F. (P. A. Herzen Oncol. Res. Inst., Moscow). Vop. Onkol. 9(11):26-30, 1963.

The extracts of normal and sarcomatous human tissues as well as sera of sarcomatous pts. served as antigens to study the anaphylactic and

desensitizing reactions in guinea pigs. After sensitization with tumor material the admin. of normal tissue antigens caused anaphylaxis in 57/68. This indicates the presence of identical antigen in both the sarcomatous and normal tissue. Sensitization with antigen of one sarcoma and desensitization with another led to anaphylactic reactions in 14/20, thus suggesting the presence of identical antigens in different kinds of sarcomas. Only 4/14, sensitized with cancer antigen and desensitized with sarcoma antigens and vice versa responded anaphylactically. Sensitization with sarcoma or blood serum antigens of sarcomatous pts. and the desensitization with normal human sera, led to anaphylaxis in 54/66 animals receiving serum of sarcomatous pts. This proves the presence of different antigens in normal and sarcomatous blood sera in man.

64-1820 ON MALIGNIZATION OF MULTIPLE STOMACH ULCERS. (Rus.) Danilenko, M. V. (De Clin. Surg., N. I. Pirogov Inst. Med., Vinnitsa Ukrainian SSR) and T. A. Kadoshchuk. Vop. Onkol. 9(11):87-91, 1963.

A case is described of a 41-year-old man in whom 4 primary cancer foci developed from 4 chronic gastric ulcers. The pt. had been suffering for 10 yr. from a gastric ulcerous disease. On the basis of this observation the authors suggest the possibility of simultaneous primary malignization of multiple chronic gastric ulcers. The diagnosis of such multiple gastric ulcer malignization is difficult. (Author summary)

64-1821 INCIDENCE OF TUMOURS IN RATS GRAFTED WITH SPLEEN FROM DONORS TREATED WITH EXTRACTS FROM THE WALKER TUMOUR. (E.) Medzihradský, J. (Inst. Cancer Res., Bratislava Czech.). Neoplasma (Bratisl.) 10(4):447-448, 1963.

Walker tumor tissue, removed 18 days after the original implantation into Wistar rats, was kept frozen until needed. A group of male, adult Wistar rats was immunized with 5 weekly doses of a high speed supernatant of this material, inj. into various sites and i.v. No tumors developed in these animals during a period of 3-4 mo. Twelve wk. after start of immunization, one rat was killed, its spleen was sliced and 5 male Wistar rats each received 5 grafts evenly distributed over the abdominal cavity. After 15 wk., 3/5 developed identical spindle-cell fibrosarcomas (in one of the 3 rats the spleen graft was rejected). Other studies are under way to rule out possible poliovirus infection and to verify possible tumor induction by biological material in the isologous spleen graft of donors pretreated with tumor tissue.

64-1822 AUTORADIOGRAPHIC INVESTIGATIONS ON PHYSIOLOGIC, REPARATIVE, AND PATHOLOGIC

REGENERATION. (Ger.) Oehlert, W. (Inst. Path., Freiburg/Br., Germany). Pp. 525-543 in Radioaktive Isotope in Klinik und Forschung. (Radioactive Isotopes in the Clinic and Research. Vol. 5). Reports of the International Symposium in Gastein, 1962. Fellingner, K. and W. Oehlert (Eds.). Urban and Schwarzenberg, Munich, 566 pp., 1963.

Physiological regeneration of the stratified squamous epithelium and of the mucous membranes of the gastrointestinal tract has been studied with H^3 -thymidine by autoradiographic techniques in the white mouse. It could be shown that only the cells of the intermediate zones are able to synthesize DNA. In these zones the multiplication of the cells produces 2 types of cells with different potentials. One type of cell becomes a postmitotic cell, losing its ability for further DNA synthesis, and migrates to the surface of the tissue. The daughter cell remains an undifferentiated cell and remains in the indifferent zone. This cell retains its ability for further DNA synthesis and multiplies with a certain lifespan. The other type of cell has a different mean life span. The relation of the life span of these two cell types is constant, in a steady state, and is characteristic for each tissue investigated. A unidirectional change in the lifespan of one cell type leads to a change of the cell population, the total number of cells remaining constant. Each change of only one cell type leads to a change of the total number of cells. The mechanism of hyperplasia and cancerization in experimental skin carcinoma of the mouse was studied by autoradiographic examinations. In cancerization, under increasing diminution of the life span of the intermitotic cells, the frequency of these cells for unequal cell division increases. This mechanism begins in the reticular zone. This zone can therefore be called the site of initiation of the cancer. Further autoradiographic examinations have been performed on the regenerating rat liver following partial hepatectomy. It could be shown that DNA synthesis increases in certain areas of the lobule and then spreads out over the whole liver tissue. It is concluded that polyploidy is the reason for the increase of continued increased DNA synthesis after the mitotic activity had decreased. (Author summary)

3 ISOANTIBODIES TO HUMAN CANCER CELLS IN HEALTHY RECIPIENTS OF CANCER HOMOTRANSPLANTS. (E.) Itoh, T. (Sloan-Kettering Cancer Res., New York) and C. M. Southam. Cancer Res. 23(4):469-483, 1963.

Transplants of 9 cancer cell lines and 2 normal cell cultures were made in 20 healthy volunteers. Each man was given only one type. Sera collected before and 2, 4 and 6 weeks after implantation were studied using the erythrocyte agglutination technic with sera prepared as saline extracts of freshly

harvested cells of 10 cancer cell lines and 8 cell lines of normal origin. All pretransplantation sera gave negative tests. Two recipients of normal cell transplants produced no antibody which could be detected with normal cell test antigens, and very rarely showed low level reaction with cancer cell antigens. All 18 recipients of cancer cell lines had antibody in the 2- and 4-week serum specimens but seldom in the 6-week serum. These sera reacted against the cell type transplanted and almost equally as well against other cancer cell lines of various types. Several reacted with the "transformed" FL amnion cell line but reactions with other cells of normal origin were rare. Reproducibility of titers on repeated tests was good. Following adsorption of these sera with fresh cell suspensions prepared from tissue cultures, blood, or tissue specimens, they were retested against cancer cell antigens. In most instances antibody titers were not significantly affected when the adsorbing cells were normal but disappeared when cancer cells were used. The data demonstrate that the 10 cancer cell lines which were studied contain an antigen or antigens in common which were foreign to the transplant recipients and rarely detectable in the normal cell lines and normal tissues which were studied. These results are consistent with the concept of human cancer-specific antigens common to the cancers of many individuals. There are, however, other plausible explanations. These are discussed and the need for caution in interpretation of antigenic analyses based on antibody formation to homografts (or heterografts) is stressed. (Author summary)

64-1824 APPRAISAL OF SEVERAL BIOLOGICAL PROPERTIES OF EHRlich ASCITES TUMOR TO MALIGNANCY. (E.) Tsukada, H. (Cancer Res. Inst., Sapporo Med. Coll., Hokkaido, Japan), S. Fujiwara, M. Ezoe and F. Fujiwara. Gann (Jap. J. Cancer Res.) 54(3):311-321, 1963.

Survival time of the host mice, multiplication of the tumor cells in ascites, hemorrhage into ascites, accumulation of ascitic fluid, tumor cell infiltration into abdominal viscera of mice, and solid tumor formation in the lung of mice after i.v. tumor cell inoc. were compared using hyperdiploid, hypertriploid, and hypotetraploid lines of Ehrlich ascites tumor. Malignancy of these tumor lines was found to increase in the order of the hyperdiploid, hypotetraploid, and hypertriploid tumor in terms of the smallest size of inoculum required for giving rise to the critical survival time of mice, which conceivably expresses the magnitude of malignancy. It was concluded that none of these properties were directly related to the death of the host. Correlations between these properties and malignancy of the tumor was discussed in detail. (Author summary)

64-1825 ENDOREPLICATION IN A PATIENT WITH ACUTE MONOCYTIC LEUKAEMIA. (E.)

Reisman, L. E. (Child. Res. Ctr. Michigan, Detroit), W. W. Zuelzer and M. Mitani. Lancet 2:1038-1039, 1963.

In a 7-year-old girl with acute monocytic leukemia a large number of cells with endoreduplication was found both in peripheral blood preparations (19/120 cells examined) and in marrow preparations (12/59 cells examined). The major (85%) portion of the cells of the marrow were of an aneuploid stem-line of 47 chromosomes, the extra chromosome being a "minute", while in the blood culture preparations only 14% represented the aneuploid line. The second stem line in both marrow and blood was diploid. In the cells with endoreduplication an accurate count of chromosomes was impossible due to overlapping, but the number of chromosomes was generally in the tetraploid range.

64-1826 INDUCTION OF CARCINOMA OF CERVIX UTERI IN MICE WITH HUMAN SMEGMA. (E.)

Rao, P. S. (Dept. Path., Guntur Coll. Med., Guntur, India) and D. J. Reddy. J. Ind. Med. Assn. 41(6):280-289, 1963.

In this study the laboratory albino Swiss mice developed spontaneous mesodermal and epithelial neoplasms, but none of them developed spontaneous epithelioma of the cervix. 20-Methylcholanthrene implantation into the cervixes of these mice induced epithelioma in 46.15%. These observations support the view that the cervicovaginal epithelium of our stock of mice is prone to malignant transformation. Varying grades of localized cervical epithelial hyperplasia, in particular basal cell hyperplasia of a localized and irregular nature, was observed in smegma-treated virgin mice which was distinctly different from the mild diffuse hyperplasia observed in saline-treated controls. Epithelial hyperplasia was marked when smegma was inj. intravaginally at less frequent intervals with increasing quantity of smegma. In smegma-treated mice, 4/44 (9.1%) developed epithelioma of the cervix in an av. period of 549.9 days with an av. dry wt. equivalent to 731.6 mg. In 22 mice treated with 10 mg dry wt. equivalent of smegma admin. at 5 days' interval, 3 developed epithelioma of the cervix. When a lesser quantity of smegma was inj. at more widely spaced intervals of time, epithelioma could be induced in 800 days with 606 mg of smegma. This study confirms the fact that the constantly associated cervicitis in the smegma-treated mice plays a contributory role in the production of proliferative changes in the epithelium of the cervix. (Author summary)

64-1827 RELATIONSHIPS BETWEEN BLOOD GROUPS AND CANCER IN E. N. T. (Sp.)

Bartual Pastor, J. (Otorhinolaryng. Clin., Fac. Med. U. Valencia, Spain). Acta Otorinolaring. Iber. Am. 14(3):312-322, 1963.

In a study conducted during 1961-1962, distribution of 70 cancer pts. in blood groups "O", "A" and "B", was, resp., 55.7%, 34.3% and 10.0%. Similar distribution of 58 pts. with cancer of larynx was 50.5%, 37.9% and 12.0%. In Valencia the largest blood group in the general population is "A" (46.6%) then "O" (39.2%). The author believes that the greater or lesser incidence of a cancer in one blood group or another does not indicate a cause and effect relationship.

64-1828 RELATIONSHIP BETWEEN THE ABO BLOOD GROUPS AND VARIOUS TYPES OF CANCER.

(Rum.) Ionescu, V. T. (Inst. Oncol., Bucharest, Rumania) and A. Caratzali. Oncol. si Radiol. 2(1):57-64, 1963.

In a statistical study compiled from observation on 5,000 cancer pts. as compared with 15,635 healthy subjects, the authors have found that occurrence of blood group O was more frequent in pts. with cancer of the stomach, breast, vulva and vagina and also in leukemia and bone sarcoma. Group B was more frequent in pts. with cancer of the nasopharynx, lung and breast. Group A was less frequent than in normal subjects in pts. with cancer of the breast and bone sarcoma; group A was less frequent in all types of cancer, excepting bone sarcoma and Hodgkin's disease. For all other types of cancer, the frequency of ABO groups was within the range of deviation for normal subjects.

64-1829 ABO BLOOD GROUPS AND MULTIPLE CANCER (E.) Fadhli, H. A. (U. Texas Med. Branch, Galveston) and R. Dominguez. J.A.M.A. 185(10):757-759, 1963.

A statistically significant excess of blood group A has been found in a sample of 123 white pts. with multiple primary cancers. This sample represents 2.4% of all pts. with cancer in a 20-year survey. In 54% of the pts., the first and last diagnosis of cancer occurred within 3 yr. of one another. The relative frequency of sites of the cancers, taken individually, does not differ essentially from that of single cancers. No statistically significant difference was found between male and female with respect to the ABO system. (Author summary)

64-1830 BLOOD GROUPS AND CANCER. (Sp.) Estevez, R. A. Sem. Med. 122(30):1121-1128, 1963.

Based on a study of 1,023 pts. with neoplasms, the author reports an excess of cancer in blood group A, compared to a control group of 21,715. This excess was especially marked for cancer of the stomach.

1831 BLOOD GROUPS OF PATIENTS WITH GASTRIC CANCER. (Rus.) Chubina, A. P. (Dept. Path. Physiol., 1st Moscow Med. Inst. (Order of Lenin), USSR). Vop. Onkol. 9(8):18-23, 1963.

The distribution of blood groups among Russian stomach cancer pts. (930 cases) and volunteers was studied. In all cases stomach cancer was histologically confirmed. The influence of sex, age, accompanying achylia and tumor localization was taken into consideration. No difference in blood group distribution was noted among the sexes. Among the females suffering from stomach carcinoma with accompanying achylia, there was a marked increase of the frequency of blood group A (I) and a decrease of incidence of blood groups B (II) and B (III) compared to controls. The greatest decrease in frequency was noted for blood group B (III). The differences, however, were not statistically significant. (Author summary)

1832 BLOOD GROUP OF PATIENTS WITH CARCINOMA OF THE UTERUS. (It.) Chisale, E. (Malliera Hosp., Genoa, Italy). Pathologica 825-826):133-135, 1963.

A survey on the distribution of ABO groups in cases of uterine cancer, the author observed a higher frequency of A group when compared with a group of 1275 subjects chosen among the Ligurian population. (Author summary)

1833 INVESTIGATIONS ON SERUM FACTORS Gm(a), Gm(b) AND Gm(x) IN CANCER PATIENTS. (Fr.) Saracino, R. (René Huguenin Hosp., Saint-Cloud, France), A. Eyquem, Podliachouk, I. Lille and P. Gabay. Bull. Acad. Franc. Cancer 50(1):123-138, 1963.

Analysis of serum from 995 pts. with cancer (including 379 of the uterus and breast) for Gm(a) and 500 cancer pts. for Gm(b) and Gm(x), no difference in frequency of the Gm groups were found compared to 201 controls. In 179 cases of rhinolaryngologic malignant tumors, there was no appreciable difference in distribution of Gm(a) groups. Out of 43 cases of blood malignancies, 3 cases were found of Gm(a-, b-, x-) phenotypes, as well as a decrease in the Gm(a) group frequency. Upon analysis by paper electrophoresis of serum from Gm(a-) pts. smaller amounts of γ -globulins were found than in Gm(a+) pts. There was also a decreased frequency of Gm(a) factor in cases of connective tissue cancer.

1834 THE BIOCHEMICAL LIPID SYNDROME AND VASCULAR ELASTICITY IN SMOKERS. (Rum.) Ionescu, M. (Inst. Int. Med., Rumanian Acad. Sci., Bucharest), V. Dobreanu-Enescu, C. Molner, Teodorini and M. Lazarovici. Stud. Cercet. Intern. 4(4):535-537, 1963.

The hemodynamic values and biochemical deter-

The hemodynamic values and biochemical determinations (cholesterol, lipemia, the Kunkel reaction, β/α lipoproteins) performed on 40 smokers and 40 nonsmokers did not reveal any significant differences between the two groups.

64-1835 MULTIPLE TUMORS OF THE STOMACH. (Rus.) Elanskii, N. N. (Clin. Surg., 1st Moscow Med. Inst. (Order of Lenin), USSR). Khirurgiia (Moscow) 39(6):20-26, 1963.

In a study based on the literature and the review of 5,000 of his own cases of gastric resection performed in a 15-year period, the author feels that the process of carcinogenesis in the stomach is multicentric. As a rule it is the result of the transformation of benign into malignant lesions, although polyps and ulcers can be found side by side with cancer. While 4 case histories are presented to support this theory, the author stresses the difficulty of proving such transformation histologically. To illustrate the ability of epithelial cells to undergo malignant change, the skin cancer on hands of radiologists is cited. This is preceded by dermatitis, eczema and papillomatosis. As the malignant tumor can be of various grades and degrees (adenocarcinoma to solid cancer) so can the surrounding cells of the mucous membrane be in various stages of malignant change. (See also CRA 1(9-10): #1820, 1964.)

64-1836 THE EFFECT OF INJECTIONS OF CELL SUSPENSIONS ON CHEMICALLY INDUCED CARCINOMA IN THE RABBIT. (Ger.) Schnitzer, A. (Birmensdorferstr. 1, Zurich, Switzerland). Oncologia (Basel) 16(3):196-207, 1963.

Six rabbits with chemically induced tumors on flank and ear were inj. i.m. with dried spleen cells (4 doses each about 35 mg variously spaced from 3-6 wk.). Approx. 2½ mo. after the experiment was begun, macroscopic changes began to appear. Part of the tumors regressed; others increased in size and circumference, becoming large, soft, partially erosive degenerating tumors. Histologic studies at 3 and 4 mo. showed profound morphologic alterations. The deeply proliferating strands of carcinomatous tissue disappeared, supplanted by connective tissue. Later this became a massive, disorganized, excessive overgrowth of connective tissue elements. This development seems to constitute a defense reaction, indicating an altered metabolic state of the connective tissue induced by the carcinogen. There are indications that the altered metabolic conditions of the connective tissue play an important, if not a decisive, role in the carcinogenic process.

64-1837 ATTEMPT AT HOMOLOGOUS TRANSPLANTATION OF MONKEY TUMORS. (Rus.) Nadareishvili, A. E. (Inst. Exptl. Ther. Path., Acad. Med. Sci. USSR, Moscow) and G. N. Zantariia. Ark. Pat. 25(7):32-37, 1963.

Ten different tumors (7 induced by radioactive isotopes and 3 spontaneous) from monkeys were transplanted into other monkeys (chiefly rhesus). Despite conditioning of the recipients with cortisone, X-irradiation, denervation or intra-hepatic sensitization, no growth occurred except for 1 spindle cell osteogenic sarcoma. This tumor was transplanted in 2 generations of cortisone-treated monkeys with the development of tumors in 4/9 and 8/14, resp. Ultimately all tumors were resorbed; homotransplantation of the second generation failed, despite treatment of recipients with cortisone.

64-1838 ORGAN DISTRIBUTION OF NEOPLASMS OF THE LYMPHATIC AND BLOOD-FORMING TISSUES, AND THEIR CLASSIFICATION IN THE INTERNATIONAL REGISTER OF DISEASES, INJURIES AND CAUSES OF DEATH. (Ger.) Wildner, G. P. (Inst. Path., Humboldt-U., Berlin) and T. Umbreit. Arch. Geschwulstforsch. 21(1):50-60, 1963.

On the basis of the organ distribution of 3,896 cases of neoplasms of the lymphatic and blood forming tissues in the Cancer Disease Statistics of the German Democratic Republic, it is demonstrated that the predominantly histologic classification of these neoplasms in the International Register of Diseases, Injuries and Causes of Death under the numbers 200 to 205 minimizes the information about their organ frequency. Almost a third of the lymphosarcomas and more than half of the

reticulosarcomas are localized in organs, of which the other malignant neoplasms are classified under other numbers, according to the International Register. The best way is the classification of neoplasms according to their histologic structure and their location, as has already been described in the cancer statistics of the German Democratic Republic and many other countries. (Author summary)

64-1839 THE CLINICAL USE OF BCG VACCINE IN STIMULATING HOST RESISTANCE TO CANCER. (E.) Villasor, R. P. (U. Philippines Coll. Med., Manila), M. S. A. Fetalino and A. T. Ramirez. Philipp. J. Surg. 18(2):85-96, 1963.

The tuberculin reaction of 187 randomly selected pts. with different histologic types of cancer was tested and studied in relation to the stage of the disease. The control group consisted of 185 unselected surgical pts. Depression of tuberculin sensitivity, indicating depressed cellular immunity, was found in a surprisingly large proportion of cancer pts., even in the earliest stage. This finding may serve as a significant lead in probing into the mystery of how cancer begins to destroy the host. It establishes the rationale for the clinical use of RES stimulants, like BCG vaccine, as an adjuvant that might possibly enhance the effectiveness of the known therapeutic modalities (See also CRA 1(9-10):#1809, 1964.) (Author summary)

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration(s)	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health, USA
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit(s)
e.g.	for example	ppm	parts per million
FFU	focus forming unit(s)	pt.(s)	patient(s)
g	gram(s)	RBC	red blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
ID ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution(s)
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit(s)
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose(s)	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

64-1840 SPONTANEOUS AND EXPERIMENTAL DATA ON "CANCER OF THE EYE IN CATTLE". (Fr.) Lombard, C. (Lab. Path. Anat., Natl. Sch. Vet. Sci., Toulouse, France). Rev. Path. Gen. (746): 287-315, 1963.

In a general review on the subject of basal cell epitheliomas of the eyelid in cattle incidence rates (per 1,000) are given for Normandy ranging from 10-50 in the Department of Manche to 0-1 in the Department of Eure. Precancerous lesions developed in 2/4 animals which received local inj. of a cell-free extract of an epithelioma derived from the eye of a 7-8-year-old cow. A discussion follows on the possibility that this is a virus-induced tumor, and that hereditary factors might enter into its expression. Other factors discussed included diet, trauma and UV radiation. (42 references)

64-1841 IMMUNE RESPONSES TO EXPERIMENTAL TUMORS. (E.) Boyse, E. A. (Dept. Path., New York U. Sch. Med., N. Y.). Guy Hosp. Rep. 112(3):433-448, 1963.

In a review on the present status of the knowledge of immunity to chemically induced tumor an experiment is described in which a W/Fu inbred rat was inoc. with 0.1 mg of 20-methylcholanthrene (MC) and a 3 cm fibrosarcoma was excised 6 mo. later. After 5 passages in similar inbred rats the tumor (16 mg) was reimplanted in the primary. This and similar challenges of increasing size made over the subsequent 6 mo. did not develop into tumors although some grew to a considerable size before they regressed. Another experiment describes conditions under which an MC-induced tumor did not appear antigenic when injected as a piece. If, however, cells (prepared by trypsinization in the presence of DNase) were injected in (C3H x 1)F1 male mice which had previously received a graft of the tumor which had been ligated off prior to the experiment, the second inoc. failed to take in a significant proportion of the animals (2/7 with 93,000 cells compared to 4/7 in controls not previously receiving the tumor). In BALB/c females receiving cells of a highly antigenic chemically induced tumor (derived from the same strain) 12,500 and 50 cells produced tumors in 3/3 animals in each case, but in 2/3 the tumors regressed and these animals were resistant on three different occasions to new challenges with tumor cells. In the case of leukemias (usually tested in C57BL/6 mice) there were wide cross reactions extending even to common antigenicity between spontaneous and X-irradiation-induced leukemias. Under these circumstances strong cytotoxic antibodies are formed. (24 references)

64-1842 HUMAN AND EXPERIMENTAL RADIOLEUKEMIAS. (Fr.) Duplan, J. F. (Pasteur Lab.,

Radium Inst., Curie Found., Paris). Pp. 47-59 in Cancer, Leucemie et Radiobiologie (Cancer, Leukemia and Radiobiology). Colloque Franco-Sovietique, Paris, Sept. 21-26, 1961. Gauthier-Villars, Paris, 173 pp., 1962.

In this review, a comparison of the characteristics of human and of experimental radioleukemias is drawn, including types of radiations, mode of application, dose, histopathology and biological factors. (17 references)

64-1843 COMPARISON OF PROPERTIES OF TWO VIRUSES--SV 40 AND POLYOMA VIRUS--ONCOGENIC FOR HAMSTERS. (E.) Eddy, B. E. Pp. 138-158 in Perspectives in Virology III. The Gustav Stern Symposium. Pollard, M. (Ed.). Hoeber Med. Div., Harper and Row Publ., Inc., New York, 292 pp., 1963.

In a review of the literature and work from the author's laboratory, the properties of the two viruses are compared in terms of the type and time of appearance of lesions as well as of the doses and other conditions which are required for production of tumors in hamsters. In other studies cited, after SV40 virus was given, no tumors were observed in the mouse (529 days), rat (437 days), rabbit (213 days) and guinea pig (444 days). Polyoma virus does induce tumors in all these animals, but less quickly than in the hamster. Both viruses grow in cell cultures prepared from more than one animal species, yet each virus produces characteristic cytopathic changes which lead to complete cell destruction in only one species. Some of the problems involved in the growth, transmission and identification of the viral agents were also brought up in a discussion of the paper. (37 references)

64-1844 HYPOTHESIS OF THE REGRESSIVE EVOLUTION OF TUMOR CELLS. (E.) Olenov, Yu. M. (Inst. Cytol., USSR Acad. Sci., Leningrad). Fed. Proc. 22(3):T557-T564, 1963.

A hypothesis for the evolution of tumor cells is presented which derives mainly from various regressive changes which occur in the organization of differentiated cells with eventual alteration to partial autonomy. The various influences which bear upon selection in this process are examined. (59 references) Originally published in *Tsitologiya*, 4(3):251, 1962.

64-1845 VIRUS AND CANCER. (Por.) Gorescu, D. I. (Cancer Res. Assn., Sao Paulo, Brazil). Rev. Brasil Cir. 45(5):364-369, 1963.

A review of the evidence available in the literature which leads the author to consider cancer as viral in origin. (34 references)

- 64-1846 WIDESPREAD PERSISTENCE OF FILTRABLE AGENTS IN TRANSPLANTABLE TUMORS. (E.) Hamazaki, Y. (Dept. Path., Okayama U. Sch. Med., Japan). Bull. Cancer Inst. Okayama Univ. 2(2): 1-122, 1962.

An extensive review is presented, mostly of the work of the author and his colleagues, on the presence of filterable agents, both carcinogenic (FAC) and noncarcinogenic (FANC) in a wide variety of tumors, with special emphasis on studies with various strains of Yoshida tumor (virus HST). Immunologic studies with HST are also presented. By the feeding of tumor tissues, tumors have been produced in extra-intestinal sites. Thus, on the basis of studies both on the inoc. of the two types of agents and the induction of extra-intestinal tumors (EIT) by oral feeding, 26 tumors and strains were classified into 4 types: type A, + for FAC and FANC, also + for EIT (rabbit myxoma), negative for EIT (chicken sarcoma). Type B is negative for FAC, + for both FANC and EIT (HST, Brown Pearce carcinoma, *et al.*); type C is negative for FAC and EIT, + FANC (R111 mouse mammary cancer, Sarcoma 180, *et al.*; type D is negative for FAC, FANC and EIT (chemically induced fibrosarcoma and nontransplantable tumors). (121 references)

- 64-1847 THE DEVELOPMENT OF EXPERIMENTAL TUMOURS IN THE LUNGS OF VARIOUS LABORATORY ANIMALS. (E.) Gričiūte, L. (Res. Inst. Oncol., Min. Health, Lithuanian, SSR). Acta Un. Int. Cancr. 19(3-4):687, 1963.

With the use of radioactive isotopes and chemical carcinogenic substances, lung tumors can be induced in various experimental animals; tumor formation is preceded by multiple proliferative changes of the bronchial and alveolar epithelium. From the histogenetic point of view, these tumors show differences: in rabbits and mice they are alveologenic, in rats they are bronchial and most closely resemble human lung cancer. Thus the tumorigenic reaction of the tissues in various species of animals is different. (No references)

- 64-1848 TRANSFORMATION OF CELLS IN VITRO BY VIRUSES. (E.) Dulbecco, R. (Salk Inst. Biol. Studies, San Diego, Cal.). Science 142: 932-936, 1963.

Reviewed are studies of the changes involved in viral transformation in cell cultures, including changes in contact sensitivity and in growth regulatory processes. Although transformed cells are not always simultaneously cancer cells, the difference may be merely an operational one, due to the appearance of new surface antigens possibly leading to rejection in isologous hosts. Characteristics of cancer producing viruses are discussed under 2 classes, RNA viruses which cause leukemias and solid tumors in chickens and rodents, and DNA viruses producing solid tumors,

mainly in rodents. In the last group, virus multiplication is usually in the nucleus, and on exposure of a cell population to the virus some cells die and produce virus, others become transformed. The recently reported circularity of the DNA of polyoma virus, possibly also of the papilloma and related viruses, and of some temperate but not of virulent bacteriophage DNA's suggests that for DNA viruses such a circular form would offer stability, ability to synthesize gene products, and at the same time prevent multiplication. Much remains to be learned about the state of viral RNA in RNA virus-transformed cells, and at this time it is unclear whether the RNA can enter into some kind of integrated state in the cells. (33 references)

- 64-1849 CHROMOSOMES AND CARCINOGENESIS. (E.) Stich, H. F. (Dept. Biol., Queen's U., Kingston, Ontario, Canada). Canad. Cancer Conf. 5:99-115, 1963.

A detailed review and discussion is presented to support the genetic concept of carcinogenesis. However, it is admitted that not every neoplasm must follow the pattern involved in this concept, e.g., mitotic irregularities, heterogeneous cell population, and clone formation by cells with an abnormal chromosome complement. The existence of neoplasms transmissible over several generations as an aberration of a single gene clearly illustrates a different mechanism. The unresponsiveness of cells to a mitotic stimulus which develops during the process of carcinogenesis might point to a mechanism which permits cells to escape the growth-controlling mechanism of the body. (See also CRA 1(11):#1894, 1964.) (77 references)

- 64-1850 CELL-CELL INTERACTIONS IN VITRO: THEIR RELATION TO DIFFERENTIATION AND CARCINOGENESIS. (E.) Siminovitch, L. (Dept. Med. Biophys., U. Toronto, Canada) and A. A. Axelrad. Canad. Cancer Conf. 5:149-165, 1963.

In an attempt to explain why tumor cells often closely resemble the embryonic cells from which the tissue originated, a review is presented of recent work (mostly in vitro) concerning the effects on cell properties and behavior of (1) changes in spatial relations among cells, (2) cell fusion, and (3) virus infection. (65 references)

- 64-1851 HEREDITY AND THE ETIOLOGY OF NEOPLASMS. (E.) Hadley, H. G. (Hadley Mem. Hosp., Washington, D. C.). Geneesk. Gids. 41(20):401-404, 1963.

A review and discussion of the etiology of neoplasms (see CRA 1(5):#783, 1963). (No references)

- 64-1852 HEREDITY AND THE ETIOLOGY OF NEOPLASMS. (E.) Hadley, H. G. (Res. Found. Inc.,

Washington, D. C.). J. Egypt. Med. Assn. 46(2): 169-176, 1963.

See CRA 1(11):#1851, 1964. (42 references)

4-1853 GENETICS OF TUMORS. (Ger.) Verschuer, O. v. (Inst. Human Gen., Münster, Germany). Internist (Berlin) 4(9):392-397, 1963.

In a review of recent statistical studies of the familial incidence of cancer, including studies of monozygotic and dizygotic twins, the author concludes that genetically determined predisposition to cancer is seen only in a few, rare forms of the disorder and a few, rare precancerous conditions: e.g., retinoblastoma, polyposis coli, xeroderma pigmentosum. However, a genetically determined organ susceptibility to cancer is now considered possible as concerns mammary carcinomas and those of the corpus uteri, ovaries, stomach and prostate. Results of familial studies and studies of twins are inconclusive as regards a similar susceptibility existing for carcinomas of the cervix uteri, esophagus, or bladder. Probably involved are hormonal influences, particular antigens to certain blood groups, or a specific tissue susceptibility due to as yet unknown causes. He cautions that the susceptibility in question does not imply an increased likelihood of becoming cancerous, but rather an increased likelihood of a specific organ being involved if cancer does occur. (36 references)

4-1854 CHROMOSOME MUTATIONS AND SOME OF THEIR RELATIONSHIPS TO THE CANCER PROBLEM. (Ger.) Rieger, R. (Res. Inst. Plant Culture, German Acad. Sci., Gatersleben-Berlin). Zschr. Biol. 56(8-9):511-524, 1963.

A general review of studies of chromosomal mutations in cancer cells, some agents involved, and possible mechanisms of action which have been postulated. (No references)

4-1855 SMOKING AND CANCER OF THE STOMACH. (Ger.) Schmähl, D. Deutsch. Med. Wochenschr. 88(45):2207-2208, 1963.

In a cursory review of published findings, the author concludes that animal-experimental studies argue against a causal connection between smoking and cancers of the stomach, although the possibility has not yet been excluded that smoking may be one of a number of simultaneously acting factors the combined effect of which could lead to carcinogenesis. (11 references)

4-1856 OCCUPATIONAL CANCERS OF THE RESPIRATORY ORGANS. (E.) Hueper, W. C. (NCI, Bethesda). Pp. 147-177 in Advances in Cardio-Respiratory Diseases. Vol. 1. Selected Lectures

from the 1961 Series of the Am. Coll. Chest Phys. Banyai, A. L. and B. L. Gordon (Eds.). Year Book Med. Publ., Inc., Chicago, 359 pp., 1963.

In a comprehensive review the author describes recognized occupational respiratory carcinogens, including arsenic, asbestos, chromium, nickel, isopropyl oil, mustard gas, coal tar, mineral oil and radioactive chemicals, and also the carcinogenic effect of some of these agents on non-respiratory organs of humans and of experimental animals when introduced by routes other than inhalation. Tabulated are the histologic types of occupational lung cancers (frequency of squamous cell carcinoma = 40%; controls, 29%), the attack rates, the latent periods, and the age distribution. It is concluded that occupational respiratory carcinogens may induce cancers of practically any histologic type, with an incidence and length of latent period roughly proportional to the duration and intensity of exposure, and also to the relative potency of the agent, and the reactivity of the host organism. The exposure conditions prevailing in the production of occupational cancers favor their occurrence at an earlier age period than that seen for cryptogenetic lung cancers. No adequate human or experimental evidence exists for the establishment of a minimal effective dose. (38 references)

64-1857 THE MAGNITUDE OF THE LUNG CANCER PROBLEM IN CANADA. (E.) Davies, J. W. (Epidemiol. Div., Dept. Natl. Health Welfare, Ottawa, Ontario, Canada), C. B. Walker and E. W. R. Best. Canad. Med. Assn. J. 89(21):1084-1091, 1963.

Morbidity data, lung cancer mortality in specified countries, and the high lung cancer mortality in Canada are reviewed briefly. Between 1931 and 1961 the lung cancer death rate (per 100,000) increased from 3.0 to 24.6 in males, and from 1.6 to 4.0 in females. The greatest increase in males was 18x in the 70-74 yr. age group, and in females was 7x in the 80-84 yr. age group. The lung cancer data used in the present analysis include all primary neoplasms of trachea, bronchus, and lung, plus malignant neoplasms of these organs unspecified as to primary or secondary. For both sexes combined the deaths from lung cancer in Canada during 1961 were 2774, representing 11.7% of all cancer deaths (20.3% in males, 3.8% in females). For females during the period 1931-1961 cancer death rates have shown a slight decrease from 119 to 108. (10 references)

64-1858 THE CELL SURFACE IN TUMOR VIRUS INFECTION. (E.) Vogt, P. K. (Dept. Path., U. Colorado Sch. Med., Denver). Cancer Res. 23(9): 1519-1527, 1963.

Reviewed are studies of cell surface changes after infection with medium-sized RNA viruses including avian tumor viruses, murine leukemia viruses and mammary tumor agent, and changes obtained on

infection of tissue cultures with small-sized DNA-containing tumor viruses such as polyoma and SV40. The most common change due to both classes of viruses is the occurrence of a tumor specific immunity characterized by cell mediation and by non-identity with virus neutralizing antibody. Loss of contact inhibition is another widespread change of viral carcinogenesis. An actual participation of cell membranes in tumor virus formation is found only with the RNA viruses, where the presence of cell membrane in the peripheral lipid coat of the newly synthesized virus does not appear to be a decisive factor in the loss of cell contact inhibition. However the incorporation of cell membrane components into the viral particle allows incorporation into the virus of tissue specific properties located at the cell surface. Thus cell-specific patterns mediating tissue specific adhesions could be incorporated into the virus, conferring to it a tissue tropism completely independent of the viral genome *per se*. (110 references)

- 64-1859 SENSITIVITY OF NORMAL AND NEOPLASTIC CELLS TO THE DAMAGING ACTION OF CARCINOGENIC SUBSTANCES: A REVIEW. (E.) Vasiliev, J. M. (Inst. Expl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow) and V. I. Guelstein. *J. Nat. Cancer Inst.* 31(5):1123-1150, 1963.

A review is presented of various *in vitro* and *in vivo* methods for the study of damage to cells by carcinogens. Among the methods discussed is the absorption of neutral red by liver of mice implanted with pellets of test substance; histochemical studies of alterations in the connective tissue around pellets of agent; *in vitro* studies of the effect on mitosis compared to controls; measurement of skin edema upon topical application of agent; studies of tissues during hepatic carcinogenesis and film-induced and urethan-induced carcinogenesis. Many facts indicate that neoplastic cells are often less sensitive to the toxic action of carcinogenic agents than homologous normal cells. It is suggested that this increased resistance is linked to certain essential characteristics of neoplastic cells and that further studies of the sensitivity of normal and malignant cells to the damage produced by carcinogens may be important in the elucidation of the mechanism of neoplastic change. (124 references)

- 64-1860 NEOPLASIA OF BLOOD-FORMING TISSUE IN THE CAT. (E.) Holzworth, J. (Angell Mem. Hosp., Boston, Mass.). *Ann. N. Y. Acad. Sci.* 108(Art. 3):691-701, 1963.

On the basis of autopsies performed at a veterinary hospital, neoplasms of the blood forming tissues in cats (10% in a 12-year period) appear to be more frequent than in dogs (4%). There appears to be no relation to sex and neoplasms occur in cats of all ages, some as young as 6 mo. dying with lymphoid tumors. Although the association

may be merely coincidental, episodes of anemia or of infection of some type appear in the histories of many of these cats. (67 references)

- 64-1861 CANINE NEOPLASIA. A PROTOTYPE FOR HUMAN CANCER STUDY. (E.) Prier, J. E. (Sch. Vet. Med., U. Pennsylvania, Philadelphia) and R. S. Brodey. *Bull. WHO* 29(3):331-344, 1963.

In support of the proposal that research in canine neoplasia be increased, a review is presented of some epidemiological and clinical aspects of the problem. Cancers in dogs are more frequent than in other domesticated animals; some tumor types are more frequent in certain breeds (i.e., osteosarcoma in large breeds, especially Great Danes and St. Bernards). The utility of possible genetic susceptibility awaits further critical study. Tumor types in relation to sites are outlined; where there are appropriate analogies between those in man and the dog, certain spontaneous tumors can be used for studies that are not practicable in man. (84 references)

- 64-1862 PRESENT TRENDS IN THE ETIOPATHOGENESIS OF BLOOD DISEASES AND MALIGNANT NEOPLASMS. (It.) Magrassi, F. (Inst. Spec. Med. Path. Clin. Methodol., U. Naples, Italy). *Rass. Clin. Ter.* 62(3):113-128, 1963.

A general discussion of present trends in investigations designed for the isolation of viruses from tumors and leukemias and the elucidation of the difficulties involved in the attempt to prove that any isolated agent is indeed the cause of the disease. Particular emphasis is placed on the study of murine leukemias. The author feels that Koch's postulates are perhaps not valid when applied to viruses isolated from tumors and leukemias caused by viruses due to the possible need for other unknown "conditioning" factors which determine the course of any "viral disease" in the exposed animal. (No references)

- 64-1863 IMMUNOLOGY AND SPREAD OF MOUSE LEUKEMIA: THE POSSIBILITY OF SIMILAR INVESTIGATION IN HUMAN LEUKEMIA. (E.) Sinkovics, J. G. (Dept. Med., U. Texas M.D. Anderson Hosp. Tumor Inst., Houston), C. C. Shullenberger and C. D. Howe. *Me. Rec. Ann. (Houston)* 56(9):186-188, 1963.

After a brief review of the subject of immunology and spread of leukemia in the mouse, speculations are made concerning the possible viral origin of the disease in humans. Abortive infections in human may occur which are not recognizable as leukemia. While many are exposed, the few cases that develop leukemia might be the result of several factors (high dose, emergence of virulent strains unusual way of entry, or of an infection that had occurred very early in life; also one or another of the immunological defense mechanisms of these victims might also be faulty). Areas where

sters" of cases occur deserve concentrated epidemiological and immunological studies. (6 references)

864 BACTERIA VERSUS VIRUSES IN NEOPLASIA. (E.) Hadley, H. G. (Res. Found., Inc., Kingston, D. C.). J. Egypt. Med. Assn. 45(3-4): 360, 1963.

Initially similar to CRA 1(5):#783, 1963 but more test subjects and a listing of the types of cancer involved. (31 references)

865 ENVIRONMENTAL CARCINOGENESIS IN MAN AND ANIMALS. (E.) Hueper, W. C. (NCI, Bethesda). Ann. N. Y. Acad. Sci. 108(Art. 3): 1038, 1963.

Representation is made of conclusive and suggestive evidence from the literature concerning an extension of the natural and man-made environmental hazards from man and experimental animals to domesticated and wild animals. Observations on many wild and domesticated animals are reviewed in relation to exposure to certain groups or types of suspected carcinogens: (1) aromatic amino-, nitro-, and azo- compounds; (2) coal tar and derivatives; (3) petroleum and derivatives; (4) arsenicals; (5) radioactive chemicals; (6) UV radiation; (7) lead; (8) selenium; (9) chlorinated hydrocarbons and other pesticides and herbicides (carbamates, triazole, beta-propiolactone, carbamates). Considerable emphasis is given to the use of man. Also discussed are (a) goitrogenic chemicals; (b) dietary additives, contaminants and deficiencies; (c) smegma. The paper is supplemented with 6 appendices with much additional information on specific compounds, nature of exposure and population groups involved. (317 references)

866 ETIOLOGY OF CANCER OF THE BLADDER. (Sp.) Lara Rivas, A., R. Sandoval Parra and Talancón Zapata. Rev. Mex. Urol. 22:149-152, 1963.

General review discussing the higher incidence of cancer of the bladder in workers of the chemical industry and in plants where aniline dyes are produced. Chronic irritation as a predisposing factor is also discussed. (18 references)

64-1867 ON THE HISTO-MORPHOLOGICAL CHANGES OF TRANSPLANTABLE TUMORS. (E.)

Hamazaki, Y. (Dept. Pathol., Okayama U. Sch. Med., Japan), K. Ogawa, A. Tsutumi, M. Ohmori and K. Taguchi. Acta Med. Okayama 17(1):33-50, 1963.

In a paper devoted chiefly to histological changes seen upon inoc. of chicken sarcoma virus, Brown Pearce carcinoma and Sarcoma MY, work is reviewed on the extra-intestinal tumors obtained by the oral feeding of Yoshida tumor. (See CRA 1(11): #1846, 1964.) (23 references)

64-1868 CANCER OF THE THYROID IN CHILDHOOD AND ADOLESCENCE. (E.) Root, A. W. (Dept. Pediat., U. Pennsylvania Sch. Med., Philadelphia). Am. J. Med. Sci. 246(6):734-749, 1963.

The incidence of cancer of the thyroid is reviewed in reference to age, sex, race (white and non-white), and national origin. Also reviewed are some experimental studies and the influence of X-irradiation and A bomb exposure on human thyroid cancer. (120 references)

64-1869 TUMORS OF THE URINARY BLADDER CAUSED BY CARCINOGENIC AMINO-COMPOUNDS. (Rus.) Temkin, I. S. Moskva, Medgiz, 1962.

The work presented in this book (review by G. B. Pliss, which appeared in Vop. Onkol. 9(9):123-125, 1963) represents a 25-year accumulation of material with regard to tumors of the urinary bladder in workers in the aniline dye industry. Part I of the book explains the etiological and pathogenetic instances of illness which are clinically and experimentally related to specific exposure; Part II is purely clinical and is devoted to problems of diagnosis, clinical duration, and treatment. Of special interest are the chapters in which (among others) the author discusses the problem of hemorrhagic cystitis which is not always connected with the effect of carcinogens, but may be due to the effect of noncarcinogenic aromatic compounds such as nitroaniline, dimethylaniline, etc. Of further interest is the discussion of statistical data regarding frequency of illness during contact with β -naphthylamine, benzidine, dianizidine, and 4-aminodiphenyl. Other chapters discuss chemical structure and technology of carcinogens, their metabolism, frequency of illness in various professional groups and other facts with regard to the disease. (Extensive citations indicated by the reviewer.)

See also abstract nos.: 1904, 1908, 1941, 1975

PHYSICAL CARCINOGENESIS

64-1870 CANCERS SUBSEQUENT TO RADIOTHERAPY.

(Fr.) Gricoureff, C. (Lab. Path. Anat., Curie Found., Paris). Pp. 35-46 in Cancer, Leucemie et Radiobiologie (Cancer, Leukemia and Radiobiology). Colloque Franco-Sovietique, Paris, Sept. 21-26, 1961. Gauthier-Villars, Paris, 173 pp., 1962.

Reported are 4 neoplasms (2 epidermoid epitheliomas and 2 sarcomas) detected at the site of irradiation with X-rays (2 cases) or radium (2 cases) 7-30 yr. previously. In addition 10 cases are described where cancers appeared at the site of irradiation for a tumor of a different histologic type 3.5-13 yr. after treatment. Three pts. with epidermoid carcinomas (cheek 1 case, tongue 2 cases) 4-12 yr. after irradiation developed sarcomas. Three pts., one with a myeloplastic sarcoma of the mouth, another with a neck lymph node epithelioma of low malignancy and a third with a mammary cylindroma, 9-13 yr. after irradiation developed epidermoid carcinomas. In a period of 3.5-10 yr. following irradiation treatment of epidermoid carcinomas of the uterine cervix, 3 pts. developed tumors of the body of the uterus (1 adenocarcinoma, 1 carcinosarcoma and 1 sarcoma); a fourth pt. developed a melanotic carcinoma of the abdomen with inguinal adenopathy. In a discussion of the paper Delarue, Guerin, Reverdy and Baud contributed data on radiation cancer in experimental animals and humans.

64-1871 EXPERIMENTAL APPROACHES TO NUCLEOLAR FUNCTION. (E.) Montgomery, P. O'B., Jr. (U. Texas Southwestern Med. Sch., Dallas). Exp. Cell Res. (Suppl.) 9:170-175, 1963.

Nucleolar irradiation of HeLa cells with UV microbeams resulted in a loss of nucleolar UV absorption which was already evident after 4-6 hr. and was maximal (90%) by 8 hr. When 4-nitroquinoline-N-oxide (10^{-5} M) was placed in contact with Chang liver cells for 10 min. and then replaced by fresh Hank's soln., there were nucleolar changes over a period of 4 hr., including nucleolar fusion and formation of a nucleolar cap. The latter appears to be specific for cells treated with 4-nitroquinoline-N-oxide. (See also CRA 1(3): #451, 1963.)

64-1872 MALIGNANT TUMOR FORMATION FOLLOWING SUBCUTANEOUS INJECTION OF SILICONE FLUID IN WHITE MICE. (E.) Ben-Hur, N. (Hadassah U. Hosp., Jerusalem) and Z. Neuman. Israel Med. J. 22(1-2):15-20, 1963.

Three groups of 12 one-year-old mice were given 3 ml s.c. of Dow-Corning 200 silicone fluid of viscosity (at 25°C) 20, 200 or 1,000. The fluid disappeared in 3 mice; in all others it was found under the abdominal skin. Two out of 36 developed tumors, the origin of which is probably

the skin appendages (myoepithelial cells found suggest sweat gland origin).

64-1873 X-RAY INHIBITION OF URETHAN-STIMULATED PROLIFERATION OF LUNG CELLS OF THE MOUSE AS ESTIMATED BY INCORPORATION OF TRITIATED THYMIDINE. (E.) Foley, W. A. (Dept. Path., U. Minnesota, Minneapolis), L. J. Cole, B. J. Ingram and T. T. Crocker. Nature (London) 199:1267-1268, 1963.

When the uptake of tritiated thymidine (admin. 3 and 6 hr. before killing) into lung cells was determined in control (C57LxA)F1 hybrids, labeled cells/100 grid fields remained at 26.4-33.0 throughout 10 days of observation, indicating a labeling rate of 0.44%. Animals inj. with urethane (U; 0.2 ml of 10% solution i.p.) at a dose sufficient to cause multiple pulmonary tumors in all, showed a drop in the absolute number of labeled cells on the subsequent day (8.9/100 grid fields) followed by a rise yielding 86 and 259 labeled cells on days 4 and 10, resp. X-irradiated mice (880 rads whole body) showed a transient inhibition of cell labeling with 1.0 and 0.6 cells/100 grid fields for up to days 1 and 2, followed by normal counts. When mice were treated with urethane 24 hr. before X-irradiation, the inhibition of labeling was more prolonged and was still below normal 7 days after treatment. This last suggests that U increases the sensitivity of lung cells to irradiation. The effective X-ray dose used was identical to that previously found to completely prevent lung tumor induction by U.

64-1874 BETA IRRADIATION OF RAT INTESTINE. LONG-TERM STUDIES AFTER DAILY YTTRIUM-INGESTION. (E.) Sullivan, M. F. (Hanford Lab., General Electric Co., Richland, Wash.), S. Marks and R. C. Thompson. Am. J. Path. 43(4):527-537, 1963.

Yttrium-90 was admin. in drinking water to mature female Sprague-Dawley rats for 60 days. Mortality during this period in a high-level group (av. ingestion 410 μ C/day) was 9/52; all animals experienced severe wt. loss. A low-level group of 51 (av. ingestion 91 μ C/day) showed no gross symptoms which would distinguish them from the controls. The total dose to the large intestine in the 2 treated groups was estimated to be about 55,000 and 12,000 rads, resp. Median post-treatment survival times were 350 and 434 days, resp. (controls, 626 days). In the high-level group, at autopsy 275-525 days after discontinuation of Y, 10/43 showed uterine adenocarcinomas. Oral carcinomas were seen in both groups but were more frequent in the high-level group. Corneal lesions were frequent and probably indicated direct contamination of the face. Histologic study of the intestinal tract indicated virtually complete recovery of early damage, and only 2 intestinal tumors (adenocarcinomas) were observed.

1875 THE SIGNIFICANCE OF THE TIME INTERVAL BETWEEN INTRAVENOUS INOCULATION OF YOSHIDA ASCITES SARCOMA AND TOTAL BODY X-IRRADIATION FOR TUMOR TAKE IN RATS. (Ger.) Stutz, E. (Inst. Clin. Radiol., U. Freiburg, Germany) and Schmähl. Naturwissenschaften 50(21):672, 1963.

Inoculation of 10^5 Yoshida ascites sarcoma cells, i.e., into rats of an unspecified strain resulted in 48% tumor takes localized in the kidneys, intestines, intestine, lungs, and elsewhere, but with no incidence of hepatic metastasis and actually no incidence of primary take in that organ. When total body X-irradiation preceded inoculation by 1, 2, 4, 8, or 16 days, the percentage of tumor takes was 78, 87, 90, 56, and 65, respectively. The percentage incidence of hepatic metastases rose from 0 (in inoc., non-irradiated controls) to 66, 33, 26, 27, and 3, respectively. (Differences in tumor take were statistically nonsignificant at the 8 and 16-day intervals, and at 32, and 40-day intervals in collateral experiments). The fact that takes were maximal at the 4-day interval, hepatic metastases at the 8-day interval, was taken as confirming that different organismic mechanisms of defense were involved for different organs. The authors conclude that defense against tumor take may have been a function of the whole organism, while defense against hepatic metastasis may have been organ specific.

1876 COMPARATIVE STUDY OF SARCOMA FORMATION BY IMPLANTED POLYETHYLENE FILM AND MESH IN WHITE RATS. (E.) Shulman, J. (Depts. Plastic Surg., B, Rothschild Hadassah U. Hosp., Jerusalem, Israel), T. Wiznitzer and Z. Neuman. E. J. Plast. Surg. 16(4):336-340, 1963.

Polyethylene discs 10 mm in diameter were implanted bilaterally beneath the skin of 55 white rats: those on the right side were of a polyethylene mesh of hard consistency, those on the left were of a polyethylene film of soft pliable consistency. After 18-24 mo. of 45 rats with implanted films, 4 developed tumors (8.9%); of 10 rats with meshes, one developed a tumor (10%). The authors concluded that the physical properties of the polymer seem to be responsible for its carcinogenicity, by blocking the interchange of fluids and other substances.

1877 MYELOGENOUS LEUKEMIA AND ANEMIA OCCURRING IN THE DESCENDANTS OF ALBINO RATS ADMINISTERED WITH 4-AMINO-PTEROYLGLUTAMIC ACID OR RADIOSTRONTIUM (^{90}Sr). A CONTRIBUTION TO THE ETIOLOGY OF LEUKEMIA. (E.) Setsuda, T. (Inst. Med., Kyoto U. Fac. Med., Japan), Kawahashi, K. Nishimura and Y. Inagaki. Acta Med. Univ. Kyoto 38(3):248-261, 1963.

1 mo. after the beginning of daily admin. of aminopteroylglutamic acid (A-PGA, aminopterin; 1 mg/kg i.m.) 1/9 Wistar rats developed myeloid

leukemia. Among some hybrid albino rats given daily doses of 0.01-0.05 mg/kg of A-PGA, one developed a kidney malformation; 2 showed myeloid metaplasia along with anemia. Myelogenous leukemia, splenomegaly associated with myeloid metaplasia and osteosarcoma were found in descendants of inbred Wistar rats given Sr^{90} (0.5-1.0 $\mu\text{C/g}$ body wt., s.c.). In both treatment groups there was a decrease in alkaline phosphatase activity and in peripheral neutrophils. The relationships between what is called "congenital bone marrow asthenia" and the development of anemia and myeloid leukemia are discussed.

64-1878 OBSERVATIONS ON THE CARCINOGENIC EFFECT OF ULTRA-VIOLET RAYS OF DIFFERENT WAVELENGTHS ON THE SKIN OF MICE, WITH SOME REMARKS ON CARCINOGENESIS. (E.) Waterman, N. Geneesk. Bl. X-XI:297-347, 1963.

When UV irradiation was admin. 6x/week to A. v. L. 020. strain mice kept in quartz cylinders, a lamp which emitted only rays of 253.7 m μ was practically without effect; a lamp with 73% of its output in the range of 290.0-310.0 m μ produced a high incidence of tumors; a popular lamp with 38% of its output in the range of 290.0-310.0 m μ was less potent. The skin lesions were about 60% sarcoma, about 40% carcinoma. There were marked accumulations of mast cells, mostly at the periphery of malignant tumors. There were many signs of inflammation in the dermis, infiltration by lymphocytes, dilated capillaries and fibroblasts of irregular form. In the later stages of irradiation some animals (often those without tumors) developed an allergic skin condition with severe and often fatal symptoms of "shock". The effect of concomitant application of maleinic acid anhydride 2x/wk. was doubtful because of the small numbers of animals and small dose. It was concluded that the results obtained in albino mice were not wholly comparable with those of solar carcinogenesis in man. There was a marked mutual inhibition between tumors of the skin and other spontaneous tumors in the organism (lungs). There were no typical changes in the protein spectrum of the blood of the mice.

64-1879 OBSERVATION ON THE MORE DISTANT EXPOSED SURVIVORS AMONG REGISTERED PATIENTS UNDER THE A BOMB SURVIVORS MEDICAL TREATMENT LAW IN 1957-1961 (PART I). (Jap.) Shimizu, K. (Res. Inst. Nucl. Med. Biol., Hiroshima U., Japan), M. Watanabe, S. Itoh and Y. Yamamoto. Hiroshima Igaku (J. Hiroshima Med. Ass.) 16(7):581-601, 1963.

Among the 2,246 bomb survivors who registered for medical treatment in Hiroshima during the past 5 yr., 194 were exposed at a distance greater than 3.1 Km from the hypocenter and 303 were exposed within 1.0 Km of the center. No significant relationship was observed between the distance from the hypocenter and incidence of acute symptoms.

There was a slightly higher incidence of developing neoplasms and diseases of the liver and blood forming organs among survivors exposed at a distance greater than 3.1 Km. A higher incidence of carcinoma was observed among those who entered the central area within 3 days of the bomb blast.

- 64-1880 DYNAMICS OF THE DEVELOPMENT OF BONE SARCOMAS ORIGINATING UNDER THE INFLUENCE OF RADIOACTIVE SUBSTANCE. (E.) Litvinov, N. N. Translation of Voprosy Onkologii (USSR) 1956 v. 2(3), pp. 285-294. Cited in Tech. Transl. 10(9): 1030, 1963.

After the i.p. inj. of Sr^{90} (0.4 mC/kg), rats show progressive disturbances of bone development with formation of immature and atypical bone structures. Within 2-3 mo. disturbances of osteogenesis occur manifested chiefly in the production of more incomplete fibrous and amorphous structures; later there is even greater reaction of the cellular elements culminating after 5 mo. in the appearance of tumor that fills the bone cavity and penetrates to the outside of the bone. Full translation available from Office of Technical Services, number 63-19459, at a cost of \$1.60.

- 64-1881 THE INFLUENCE OF CARCINOGENESIS DUE TO IONIZING RADIATION DURING EMBRYONIC DEVELOPMENT. (Ger.) Diener, E. (Radiobiol. Inst., U. Zürich). Zschr. Krebsforsch. 65(6): 607-619, 1963.

A control group of a tumor-free breed of young albino rats was fed 2-acetylaminofluorene (AAF). Ten-day-old embryos were exposed to irradiations of 75, 100 and 200 rad from a 31-MeV-Betatron (photon irradiation). Other 10-day-old embryos were exposed to 75, 100, 150 and 200 rad followed by postnatal feeding of AAF to the young rats (wt. 60 g). All irradiated groups showed malformations of the eyes, the nervous system and of the hind extremities; these varied with the radiation dose. In utero irradiation with doses of 75 rad led to a significant increase of AAF-induced carcinogenesis. This carcinogenesis promoting effect decreased with increasing radia-

tion dose. After 150 and 200 rad no synergistic carcinogenic effect was observed.

- 64-1882 ENDOMETRIAL CANCER IN PATIENTS PREVIOUSLY IRRADIATED FOR CERVICAL CANCER (E.) Mills, D. C. (Dept. Obstet. Gynec., Washington U. Sch. Med., St. Louis, Mo.). Obstet. Gynec. 22(3):280-285, 1963.

Among 3,181 cases of squamous cell cancer of the cervix and 852 with cancer of the endometrium diagnosed between 1935-1961 there were 3 concurrent cases. Three additional examples were diagnosed 5, 8, and 14 yr. after irradiation for cervical cancer. The present data do not permit an assessment of the carcinogenic effects on the endometrium of ionizing radiations applied in the treatment of primary cervical cancer.

- 64-1883 EFFECT OF X-IRRADIATION ON SUSCEPTIBILITY OF CELLS TO TRANSFORMATION BY POLYOMA VIRUS. (E.) Stoker, M. (Inst. Virol., U. Glasgow Scotland). Nature (London) 200:756-758, 1963.

Hamster fibroblasts, BHK21 line exposed to X-irradiation prior to and after transformation by a small plaque variant of polyoma virus showed identical inactivation kinetics. However, irradiation of normal cell suspensions yielded different proportions of normal and transformed colonies on subsequent virus infection. Thus after doses of 0, 188, 375 and 500 r, the frequencies (percent) of transformed colonies were 5.2, 8.0, 12.8, and 14.8, resp. In a similar experiment which utilized monolayers in order to avoid cell aggregation, there again was an increase in transformation frequency correlated with increase in X-ray dose up to at least 500 r. The effect was not due to aggregation of cells after polyoma virus infection yielding mixed clones of normal and transformed cells, and no evidence could be found that conditions after irradiation favored growth of transformed cells. Two possibilities are discussed, selection through irradiation of a cell type which is also more sensitive to viral transformation or an increased sensitivity to viral infection in irradiated cells.

CHEMICAL CARCINOGENESIS

4-1884 ABSENCE OF CARCINOGENIC ACTIVITY IN HIGHLY CONJUGATED AROMATIC ACETYLENIC HYDROCARBONS. (Fr.) Buu-Hoi, N.-P. (Radium Inst., U. Paris, France), F. Zajdela, K.-E. Schulte and P. Mabilhe. Bull. Assn. Franc. Cancer 50(1):105-108, 1963.

Aromatic hydrocarbons containing one or more conjugated acetylenic bonds (rich in π electrons) were inj. into C57BL/Z mice (groups of 12-13 males and 12-14 females) s.c. (0.6 mg in olive oil x3 over a period of 3 mo.). No abnormal changes or sarcomas were observed in over 400 days from diphenylhexatriene, phenylmethylhexatriene, diphenyloctatetrayne, and from two thiophene derivatives (2-phenylethynyl-5-thiophene and 2-phenylbutadiynyl-5-phenylthiophene). Testing of the first 4 compounds with several electron acceptors gave a strongly positive result only with the thiophene derivative.

4-1885 RELATIONSHIPS BETWEEN MOLECULAR STRUCTURE AND THE CARCINOGENIC ACTIVITY OF BENZOPYRIDOCARBAZOLES AND POLYCYCLIC ANALOGS. (Fr.) Lacassagne, A. (Radium Inst., U. Paris), P. Buu-Hoi, F. Zajdela, P. Jacquignon and P. Périn. C. R. Acad. Sci. (Paris) 157(4): 8-822, 1963.

Administration for up to 35 wk. to XVII/nc Z mice gastric intubation of 1.5 mg 2x/wk. (in olive oil) of 5,6-benzopyrido-(2',3'-1,2)carbazole caused gastric neoplasms in 6/16 males and 4/8 females, resp.; incidence after similar admin. of 6-benzopyrido-(3',2'-1,2)carbazole was 4/16 males and 2/8 females. Since these compounds had shown strong sarcomagenic activity on s.c. admin., other new compounds (in olive oil) were tested s.c. inj., each 0.6 mg at monthly intervals). 4 benzopyridocarbazoles, one dibenzo- β -carbazole, six naphthopyridocarbazoles and two benzo- β -carbolines, two had sarcomagenic activity: 5,6-benzopyrido-(3',2'-3,4)carbazole and 6-benzopyrido-(2',3'-1,2)carbazole, causing sarcomas in 7/14 and 9/15 mice, resp.

4-1886 INHIBITORY EFFECTS BY ALPHA-NAPHTHYL-ISOTHIOCYANATE ON THE DEVELOPMENT OF HEPATOMA IN RATS TREATED WITH 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE. (Jap.) Sasaki, S. (Inst. Path., Nara Coll. Med., Japan). Nara Igaku Zasshi (J. Nara Med. Assn.) 14(2):101-115, 1963.

Feeding of α -naphthyl-isothiocyanate (ANIT; 0.1%) 10 wk. preceding the feeding of 3'-methyl-4-dimethylaminoazobenzene (0.06%) for 24 wk. resulted in a lower incidence of hepatomas (2/23) compared to controls receiving the carcinogen only (21/30). Similar lowering of incidence of tumors (3/24) was found when the two agents were fed simultaneously for 24 wk. The tumors which did develop in ANIT-treated animals were

usually single and small compared to controls; from the histological point of view they were hepatocellular carcinomas and not cholangiomas.

64-1887 THE EFFECTS OF ADRENALECTOMY AND PYRIDOXINE DEFICIENCY ON THE GROWTH OF 3,4,9,10-DIBENZOPYRENE-INDUCED TUMORS. (E.) Benton, D. A. (Roswell Park Mem. Inst., Buffalo, N. Y.). Cancer Res. 23(7):1016-1020, 1963.

Studies are reported on the growth of tumors induced in male HaICR Swiss mice by the inj. of 3,4,9,10-dibenzopyrene (0.4 mg in 0.2 ml of sesame oil, s.c. in the right axillary region). Adrenalectomy resulted in regression of 43% of small tumors, others decreased in diameter; most resumed growth between wk. 6 and 10. About 14% remained tumor-free for more than 12 wk. Tumor growth was temporarily inhibited by a pyridoxine-free purified diet which was not related to caloric restriction. It is not known at this time whether the impaired growth is due to altered metabolism of the tumor or to a host response to the tumor.

64-1888 CARCINOGENESIS AND ADAPTIVE ENZYME FORMATION. (E.) Fiala, S. (Dept. Path., Columbia U., New York) and E. Kasinsky. Neoplasma 10(2):159-165, 1963.

Male Sprague-Dawley rats fed a basal diet + twice recrystallized 3'-methyl-4-dimethylaminoazobenzene (3'-Me-DAB; 600 mg/kg of food) during a 55-day period showed a gradual but reversible inhibition of the formation of liver tryptophan pyrrolase (TPO). When 3'-Me-DAB fed animals were placed on the basal diet 3-7 days prior to sacrifice, the induced levels of TPO returned to or exceeded control levels. However, the inhibition of adaptive TPO formation was irreversible after the "critical stage" and in resulting hepatic tumors. From this and other data in the literature, it is suggested that interference with adaptive enzyme formation is the central factor in carcinogenesis. (See also CRA 1(3):#447, 1963.)

64-1889 INDUCTION OF MELANOTIC LESIONS OF THE IRIS IN RATS BY URETHANE GIVEN DURING THE NEONATAL PERIOD. (E.) Roe, F. J. C. (Dept. Exp. Path., Chester Beatty Res. Inst., London, S.W.3), D. Millican and J. M. Mallett. Nature (London) 200:1201-1202, 1963.

Injection of urethan (1 mg/g body wt., 8 weekly inj., starting at 24 hr. of life, route not stated) resulted in the appearance of "dark spots" in the eyes of 12/26 females, and of 8/25 males of the August rat strain. The lesions were discovered in 18/20 at 7 mo., with 2 more appearing by 9 mo. In 15/20 the lesions were unilateral and in 5/20, bilateral. No lesions were observed in 250 August strain controls, in 44 urethan-treated Wistar

rats, and in 50 Wistar controls. Histologically, the lesions consisted of pigmented cells containing a melanin-like substance. The cells were located in the connective tissue, contained few mitotic figures, and showed no evidence of invasiveness, suggesting nevi rather than melanomas.

64-1890 RELATION BETWEEN CARCINOGENIC POWER OF CONJUGATED MOLECULES AND THEIR INHIBITORY EFFECT ON FIXATION TO CELL PROTEINS. (Fr.) Daudel, P. (Radium Inst., Paris) and G. Prodi. *Acta Un. Int. Cancr.* 19(3-4):522-523, 1963.

Female mice of strain XVII/nc aged 6-8 mo. were painted once a day for 3 days with the noncarcinogenic hydrocarbons 1,2,3,4-dibenzanthracene (1,2,3,4-DBA) or anthanthrene (group I), with the mild carcinogens 2,10-M,7,8-benzacridine (no other description given) or 1,2,5,6-dibenzanthracene (1,2,5,6-DBA) (group II), or with the strong carcinogens 3,4-benzpyrene (BP) or 9,10-dimethyl-1,2-benzanthracene (DMBA) (group III), all in benzene, followed by extensive washing of the skin with the solvent. Subsequently the animals were painted with radioactive 1,2,3,4-DBA, 1,2,5,6-DBA, BP, or DMBA, followed by benzene washing at 24 hr., and extraction of the skin proteins for detection of hydrocarbon-protein conjugates. Response, compared to binding in controls, after application of the labeled 1,2,3,4-DBA in groups I, II and III, was, resp., 70-72, 58, and 21-47%; after labeled 1,2,5,6-DBA, 99, 106, and 14%; after labeled BP, response in group I was 128-200%, group III 20-100%; response to labeled DMBA in group I was 143%, group III 10-54%. Results appear to indicate inhibition of skin fixation in animals pretreated with carcinogenic compounds, and stimulation when pretreated with noncarcinogenic compounds.

64-1891 RELATIONSHIP BETWEEN HORMONAL SENSITIVITY OF THE MAMMARY GLANDS AND INCIDENCE OF CANCER OF THE BREAST. (Jap., Abstract) Sakakura, T. (Dept. Path., Mie Pref. Coll. Med., Japan) and Y. Nishizuka. *Nippon Naibunpi Gakkai Zasshi (Folia Endocr. Jap.)* 39(2):192, 1963.

In tests of hormonal sensitivity of the mammary glands, mice of strains C3H, BALB/cf, 129f and (C3H x 129)F1 received mammary tumor virus; none was received by strains C3Hf (ZB), BALB/c, 129 and (129 x C3H)F1. Groups of virgin, 8-week-old females were given inj. of estradiol benzoate (E; 5.0 µg) 3x/wk. for 2 mo., repeated after 1 mo. for 1 mo. more. All mice were killed 24 hr. after completion of E admin. and the right third breast was removed and assayed for hormone sensitivity. Differences in reaction to E from the most sensitive strain to the least sensitive were as follows: 129, 129f, (C3H x 129), and (129 x C3H) more than BALB/c, BALB/cf and much more than C3H, C3Hf. No relationship was seen between the effects of E and incidence of carcinoma and the presence or absence of virus. Pituitary implants from males of the same strain were transplanted

s.c. into the back of 8-week-old females (3 implants/wk. x 4) and 70 days after the last transplantation another breast was studied for hormone sensitivity. Greatest reactivity was in strains C3H and C3Hf, less but about equal reactivity was seen in strains BALB/cf and (C3H x 129); much less reactivity was seen in BALB/c, 129f, 129 and (129 x C3H). The most reaction was seen in the strains which had the higher incidences of breast cancer. The presence of virus led to a greater reaction to the pituitary transplants in strains BALB/c and (129 x C3H); there were no changes in strains C3H and 129. In strains BALB/c and (129 x C3H) virus increased the incidence of breast cancer whereas in C3H and 129 there was no change. After transplantation of pituitary tissue directly into the breast a marked increase of hormone sensitivity was observed in the groups which had received virus. These studies suggest that the mammotropin in pituitary transplants play an important role in the stimulation of carcinogenesis in mice.

64-1892 THE METABOLISM OF 1-NAPHTHYLAMINE AND ITS BEARING ON THE MODE OF CARCINOGENESIS OF THE AROMATIC AMINES. (E.) Clayson, D. B. (Dept. Exper. Path., U. Leeds, England) and M. J. Ashton. *Acta Un. Int. Cancr.* 19(3-4):539-542, 1963.

The urinary excretion of purified 1-naphthylamine (free of 2-naphthylamine) appeared to be similar, but not identical, in the dog, rat, mouse, cavy, ferret, hamster and rabbit. Analysis of derivatives of 1-amino-2-naphthol showed a higher amount of conversion (18%) than expected. This result combined with the demonstration, by paper chromatography, that appreciable quantities of 1-amino-2-naphthyl glucosiduronide were present, renders untenable the idea that the simple conversion of the aromatic amine to an ortho hydroxyamine derivative is sufficient for carcinogenic activity. (See also CRA 1(9-10):#1636, 1964.)

64-1893 TOBACCO POLYPHENOLS. IV. A COMPLEX POLYPHENOL IN FLUE-CURED TOBACCO. (E.) Runeckles, V. C. (Imperial Tobacco Co. Canada, Montreal, Quebec). *Arch. Biochem.* 102(3):354-355, 1963.

Studies are presented of the isolation and characterization of a complex polyphenol isolated from flue-cured, commercially grown tobacco. The polyphenol appears to be made up of equal parts of rutin, chlorogenic acid and scopolin.

64-1894 MOSAIC COMPOSITION OF PRENEOPLASTIC LESIONS AND MALIGNANT NEOPLASMS. (E.) Stich, H. F. (Dept. Biol., Queen's U., Kingston, Ontario, Canada). *Exp. Cell Res. (Suppl.)* 9:277-285, 1963.

Data is given for the ploidy distribution and

otic irregularities in normal regenerating liver in the rat as well as in preneoplastic liver following exposure to 3'Me-DAB (2.5 mo.) or 3 (6 mo.) and in hepatomas induced by these agents. Also presented is data on chromosome aberrations and abnormal karyotypes in the thymus and spleen of Swiss mice inj. at birth with DMBA. On the basis of this data and available data from the literature the author concludes that it is difficult to compare a preneoplastic preneoplastic cell population with that of normal tissues and to correlate biochemical changes with the process of carcinogenesis, which occur in only one out of a billion of genetically abnormal cells.

1895 CHANGE IN ACTIVITY OF SOME OXIDATION-REDUCTION ENZYMES DURING CARCINOGENESIS IN MUSCLES WITH DIFFERENT METABOLIC PATTERNS. (Fr.) Pozdniakov, O. M. (Inst. Normal Path. Physiol., Acad. Med. Sci. USSR, Moscow). Vop. Khim. 9(4):421-425, 1963.

Studies are reported on the alterations in succinate-, malate-, isocitrate-, glutamate-, cerophosphate-, and glucose-6-phosphate dehydrogenases and DPN-diaphorase activities in white and red muscles of the hen at various times after admin. of 9,10-dimethyl-1,2-benzanthracene (DBA) (see CRA 1(2):#213 and *ibid.*, (3):#453, 1963). Soon after admin. of DBA there was a significant decrease in succinate dehydrogenase activity and an increase in glucose-6-phosphate dehydrogenase. Alterations in enzyme activity were more pronounced in white as compared with red muscles. No restoration of initial enzymatic activity could be noted in white muscles up to the time of tumor formation.

1896 BEHAVIOR OF THE ELASTIC TISSUE IN THE EXPERIMENTAL CANCER-CIRRHOSIS INDUCED BY p-DIMETHYLAMINOAZOBENZENE (BUTTER YELLOW). (Fr.) Bartoloni Saint Omer, F. (Inst. Anat. Histol. Path. U. Florence, Italy). Arch. De Anat. Pat. 38(2):481-505, 1962.

In female Italic strain rats fed a diet of polished rice with the addition of p-dimethylaminoazobenzene (1.5 g/kg, in olive oil) for more than 60 days the development of liver tumors was accompanied by a marked proliferation of the elastic component of the stroma. Detailed histological descriptions are presented.

1897 THE STIMULATORY EFFECT OF 3-METHYLCHOLANTHRENE ON MICROSOMAL AMINO ACID INCORPORATION AND BENZOPYRENE HYDROXYLASE ACTIVITY AND ITS INHIBITION BY ACTINOMYCIN D. (E.) H. V. (NCI, Bethesda) and N. R. Blackburn. Biochim. Biophys. Acta 72(4):657-660, 1963.

Microsomes from 20-methylcholanthrene (MC)

treated rats (1 mg i.p. 18 hr. before sacrifice) showed 17-45% more polyuridylic acid primed incorporation of C^{14} -labeled phenylalanine into trichloroacetic acid insoluble material than microsomes from control rats. This effect was also observed with microsomes preincubated to remove endogenous RNA primer. The MC-induced stimulation of protein synthesis was prevented by inj. of actinomycin D (0.03 mg i.p. at 0, 4, 8, and 12 hr., sacrifice at 18 hr.) which inhibited the incorporation by about 30% and canceled any effect of the MC. Benzpyrene hydroxylase activity was also stimulated 18-fold in MC-treated animals (14.45 μ g of hydroxybenzpyrene formed, controls, 0.8 μ g) and the enzyme activity was reduced considerably in actinomycin D-treated rats (1.08 μ g; combined with MC 3.8 μ g).

64-1898 INFLUENCE OF DEOXYCORTICOSTERONE AND OF HYDROCORTISONE ON RAT LIVER CARCINOGENESIS BY p-DIMETHYLAMINOAZOBENZENE (DAB). (Fr.) Lacassagne, A. and L. Hurst. C. R. Acad. Sci. (Paris) 257(9):1576-1580, 1963.

In male Wistar rats simultaneous admin. of deoxycorticosterone and DAB slowed down the sequence of events leading to liver neoplasms, whereas hydrocortisone admin. continuously in the diet accelerated the early stages of DAB carcinogenesis. In both instances the histologic changes observed at various stages of carcinogenesis resembled those observed after DAB admin. to wild rats with a frequent final histologic picture of the cholangiocellular type. This was most frequent in animals receiving hydrocortisone. The authors also conclude that the various epithelial tumors observed in these livers are merely due to various degrees of cellular differentiation of clones originating during a second attempt at regeneration.

64-1899 THE EFFECT OF SIMULTANEOUS ADMINISTRATION OF RESERPINE AND OF A CORTICOID ON RAT LIVER CARCINOGENESIS BY p-DIMETHYLAMINOAZOBENZENE (DAB). (Fr.) Lacassagne, A. and L. Hurst. C. R. Acad. Sci. (Paris) 257(10):1658-1660, 1963.

Simultaneous admin. of deoxycorticosterone and reserpine increased the inhibitory activity of the hormone on DAB carcinogenesis, although reserpine by itself is known to activate DAB liver carcinogenesis in the rat. A similar inhibition was obtained in rats receiving hydrocortisone + reserpine, although either agent alone promotes DAB carcinogenesis. In DAB fed animals receiving either deoxycorticosterone or hydrocortisone the adrenals atrophied, while with the simultaneous admin. of the corticoids and reserpine this atrophy did not occur.

64-1900 RAPID LIVER TUMOUR INDUCTION BY CONFIRMED ACTION OF N-HYDROXY-2-ACETAMIDOFUORENE AND HORMONAL STIMULATION. (E.)

Pai, S. R. (NCI, Bethesda), R. S. Yamamoto and J. H. Weisburger. Nature (London) 199:1299-1300, 1963.

Male and female weanling 4-week-old rats (Fischer strain F344/N) were fed a carcinogenic diet (K) containing 0.016% N-hydroxy-2-acetamidofluorene for 13 wk. The livers of 7 male rats showed microscopic nodular hyperplasia, with 1/7 exhibiting gross enlargement, and 6/7 hypertrophy; in females 8/8 showed microscopic nodular hypertrophy, with 4 exhibiting gross enlargement, and 4 nodular livers. Among animals receiving the same diet + s.c. implants of the mammotropic tumor MtT/F4, 10/12 males and 12/14 females had carcinomas of the liver, with the remainder exhibiting nodular liver hyperplasia. Controls bearing the s.c. implant alone, or on normal diets showed no microscopic nodular hyperplasia, although in those bearing the MtT/F4 implant gross, but not microscopic liver nodular hypertrophy, was observed in 13/13 males and in 14/14 females. The promoting effect of pituitary factors are considered worthy of further investigation, especially in view of the low carcinogenicity of the diet used in the present study.

64-1901 PARTICULAR CARCINOGENIC ACTIVITY OF F-NOR-STERANTHRENE. (E.) Lacassagne, A. (Radium Inst., U. Paris), E. Buchta, D. Kiessling, F. Zajdela and N. P. Buu-Hoi. Nature (London) 200:183-184, 1963.

F-Nor-steranthrene (0.6 mg s.c. in the flank x1/mo. x 3) was admin. to female and male XVII nc/Z mice. Tumors appeared at 85-90 days in 6/7 females treated at age 3-4 mo., and included 2 mammary epitheliomas, 3 epitheliomas + sarcomas, and 1 sarcoma; at 70-90 days in 6/8 females treated at age 6 mo., including 4 mammary epitheliomas, 1 epithelioma + sarcoma, and 1 sarcoma. In males treated at 6 mo., sarcomas developed at 80-100 days in 7/7 animals. No spontaneous nor chemically induced mammary tumors had previously been observed in this strain.

64-1902 LOSS OF LIVER CELL ANTIGENS IN AZO-DYE INDUCED HEPATOMAS OF RATS. (E.) Kalnins, V. I. (Dept. Biol., Queen's U., Kingston, Ontario, Canada) and H. F. Stich. Nature (London) 200:189-190, 1963.

A total of 14 hepatomas induced in male Sprague-Dawley rats by 4-dimethylaminoazobenzene (DAB) feeding in the diet (discontinued 3 wk. before analysis) were examined for precipitin band formation on micro-double diffusion agar plates against rat serum absorbed with anti-rat liver antisera. Anti-liver serum absorbed with normal liver did not produce precipitin bands when tested against liver antigens, rat serum, or hepatomas. However, anti-liver sera absorbed with a hepatoma (H1) produced at least 5 well defined precipitin bands when tested against normal liver, but none

against rat sera, indicating that the bands represent antigens associated with normal liver. The same H1 absorbed anti-liver sera tested against the 14 hepatomas of different rats showed 1 band in 2, 2 bands in 2, and 3 bands in tumors, indicating that the number of lost antigens varies among the tumors. Considering that most, if not all, of the hepatomas employed consist of cells with an abnormal chromosome complement and/or an abnormal amount of DNA, the question is raised as to whether a correlation exists between the loss of antigens and the alteration of a genome.

64-1903 INHIBITORY EFFECT OF POLYNUCLEAR HYDROCARBONS AND AMPHENONE ANALOGS ON INDUCTION OF ACUTE ADRENAL NECROSIS BY 7,12-DIMETHYLBENZ[A]ANTHRACENE. (E.) Dao, T. L. (Roswell Park Mem. Inst., Buffalo, N. Y.) and Y. Tanaka. Cancer Res. 23(8):1148-1152, 1963.

A single feeding to rats of an effective dose of 6 polycyclic aromatic hydrocarbons including 4 carcinogens--9,10-dimethyl-1,2-benzanthracene (DMBA), 20-methylcholanthrene (MC), 3,4-benzpyrene and 1,2-benzanthracene--as well as anthracene and phenanthrene 48 hr. prior to admin. of 30 mg of DMBA completely inhibited the DMBA-induced adrenal necrosis. The minimally effective dose to induce a 100% protection for the 4 carcinogenic hydrocarbons was 10 mg, that for the 2 noncarcinogens was 25 and 100 mg, resp. Among the 4 carcinogens, MC appears to provide the most effective protection against DMBA-induced adrenal necrosis. It is interesting that a non-necrotizing dose of DMBA inhibits the necrosis-inducing effect of the same compound. Results indicate that the presence of a critical amount of adrenocortical steroids in the adrenal gland is a prerequisite to the induction of necrosis by DMBA. In the present study Metopirone was shown to be only partially effective in inhibition of DMBA-induced adrenal necrosis while o,p'-DDD, also an amphenone analog, was totally ineffective.

64-1904 TUMOR SPECIFIC IMMUNITY TO NONVIRAL TUMORS. (E.) Prehn, R. T. (Dept. Path., U. Washington Sch. Med., Seattle). Canad. Cancer Conf. 5:387-395, 1963.

After a review of both early and recent work in the field of tumor-specific antigens, some speculations are presented to help explain especially the behavior of nonviral tumors, such as those induced by 20-methylcholanthrene (20-Me). To account for the immunizing capacities of chemically induced tumors, 2 differing hypotheses are suggested: (1) Neoplasia and immunizing capacity are essentially independent in origin, their apparent relationship being due to the pressure of selection among random cellular variants. (2) Neoplasia is the direct consequence of the same cellular alterations that produce antigenicity (and thus secondarily immunizing capacity). It is held that presently available data cannot decide between these hypotheses.

re appear to be two basic but not mutually exclusive ways to look at the role of 20-Me in the induction of malignancy and antigenicity: (1) carcinogen exerts a direct chemical or physiological effect upon susceptible cells. This results in neoplasia and antigenicity. (2) The carcinogen, by interfering with the immunological mechanisms of the host allows neoplastic and antitumor cell variants to survive and eventuate in plasmas. Again the data are probably not adequate to distinguish between these hypotheses. The data which are currently being presented suggest that the second hypothesis is probably not in itself a sufficient explanation of carcinogenesis. The best evidence for the second hypothesis is that 20-Me, in the same dosages and admin. by the methods used for tumor formation, can quite definitely prevent the sloughing of male skin grafted to female C57Bl mice. Other data also suggest that suppression of the immune reaction to the carcinogen is not a sufficient cause of chemical carcinogenesis. Thus work being performed by R. Bates, appears to suggest that carcinogenesis in fibrous tissue may not be appreciably faster within the presumably protecting confines of a diffusion chamber.

1905 TUMORIGENESIS INHIBITION IN C₃H MICE. (E., Abstract) Byers, E. H. and R. H. J. Lab. Clin. Med. 62(5):864, 1963.

Attempt was made to inhibit carcinogenesis by immunizing groups of 20 isologous C₃H mice with 0.1 ml of a tissue homogenate composed of isomerase muscle, spleen and liver incubated overnight at 37°C (37) or 4°C (4) with 20-methylcholanthrene (20-Me). Two groups were inj. with Freund's adjuvant + hyaluronidase (c), two groups received only the homogenate (s). Implants of the c were inserted 21 days after immunization in the 4 groups as well as in an unimmunized control group. In groups 37-c, 37-s, 4-c, 4-s controls, av. tumor mass (unit not stated) was 8.0, 10.6, 10.7, 11.0 and 10.6. Tumor onset (days after implant) was 137.2, 121.5, 115.2 and 125.3. Percent surviving was 16.7, 22.2, 18.2 and 14.3.

1906 CHOLESTEATOMAS OF THE CAUDA EQUINA REGION DUE TO ENDOLUMBAR STREPTOMYCIN INJECTIONS. (Rus.) Volodin, N. I. (Clin. Therap., N. I. Pirogov Inst. Med., Moscow) and G. M. Kostina. Klin. Med. (Moskva) 41(9):49-53, 1963.

Case of tuberculous meningitis treated with endolumbar streptomycin inj. is reported. Five years following the treatment there occurred pain in the lumbar part of the spinal column, weakness of the muscle atrophy of the lower extremities. One year after the treatment, as a result of compression of the spinal cord by the cholesteatoma in the cauda equina region, i.e., at the site of streptomycin inj. there developed a paresis of the pelvic organs, an ascending cystopyelonephritis,

urosepsis and uremia.

64-1907 BIOCHEMICAL PROBLEMS IN EXPERIMENTAL LUNG TUMORIGENESIS BY ISONIAZID AND HYDRAZINE. (It.) Di Leo, F. P. (Inst. Path. Anat., Histol., U. Perugia, Italy) and U. Milia. Lav. Ist. Anat. U. Perugia 23(2):129-142, 1963.

The authors recapitulate the present trends in the pathogenetic interpretation of induction of lung tumors in mice through the admin. of INH [isonicotinic acid hydrazide] and hydrazine, the latter being used as a metabolite of the former. After having described some aspects of the biological activity and of the metabolism of the two substances, both *in vivo* and *in vitro*, the authors indicate that lung tumorigenesis in mice could be studied from the point of view of a specific chemical reactive group (pyridinic, aminic function, hydrazinic, carbamyl group, hydrazidic, ureidic) common to INH and hydrazine, and also from the standpoint of the detection of the metabolic route involved (formation of Schiff bases, chelating mechanism, via DPN, MAO-inhibition, anti-catalase activity).

64-1908 THE EPIDEMIOLOGY OF LEUKEMIA. (E.) Rogers, F. B. (Temple U. Sch. Med., Philadelphia, Pa.). Philadelphia Med. 59(45):1195-1200, 1963.

A review (no references) is presented which includes theories and speculations as to the etiology of leukemia throughout a long period. Changes in incidence, areas of geographic concentration, association with other diseases are discussed as well as relation to age, the occurrence of possible familial aggregation, the effect of other environmental factors and the relation to chromosome changes. M. D. Prager and S. E. Bryan recently reported a defect in aspartate transcarbamylase activity. This enzyme functions at the molecular level in leukocytes and was found to influence, through a chemical "feedback" mechanism, the production of granulocytes identical to parent cells. The blood of 9 pts. with granulocytic leukemia lacked this feedback control for cytidine, with resultant production of unlimited cytidine for daughter cells.

64-1909 DURATION AND RATE OF MITOSIS AFTER A SINGLE APPLICATION OF METHYLCHOLANTHRENE. (E.) Elgjo, K. (Inst. Gen. Exp. Path., U. Oslo, Norway). Nature (London) 200:608, 1963.

Groups of 8 hairless mice were painted with 20-methylcholanthrene (20-Me; 0.03 ml of a 1% soln. in benzene) and the mitotic count, the mitotic duration, and mitotic rate were determined weekly for 11 wk. Mitotic duration was determined by the colcemid method. A study of the data reveals that the initial increase and subsequent fluctuations of the mitotic count are obviously a

reflection of the corresponding values of the mitotic duration. The mitotic rate, however, decreases during the first 2 wk. to about half the normal value. Thereafter it displays a gradual and approx. linear increase. While the effect of a single application of 20-Me is profound, the present results do not indicate whether these variations are causally related to the carcinogenic effect of this compound.

- 64-1910 HEPATOMAS IN RAINBOW TROUT: DESCRIPTIVE AND EXPERIMENTAL EPIDEMIOLOGY. (E.) Wolf, H. (California Dept. Fish Game, Sacramento) and E. W. Jackson. Science 142: 676-678, 1963.

The Santa Monica formula dry feed diet was fed to rainbow trout (*Salmo gairdnerii*) in hatcheries in California usually for 23 mo., as a complete diet, or with single suspect ingredients removed. The number of trout with hepatomas/trouts examined on the various diets was: complete diet 24/50; less cottonseed meal 0/37; less distillers solubles 13/28; less wheat middlings 10/20. Trout in another hatchery with higher water temperature developed hepatomas in 40/50 when fed the complete Santa Monica diet, however when the diet was 85% liver + 15% cottonseed meal, hepatomas developed in 3/65, and when the diet was 85% liver + 15% distillers solubles, no hepatomas were found among 13. Results are thought to indicate that a carcinogenic ingredient is present (intrinsically or extrinsically) in cottonseed meal, and that the hepatoma inducing effect is inhibited by liver diets.

- 64-1911 GLYCOGEN-CONTAINING CELLS OF ESTROGEN-INDUCED RENAL TUMORS OF THE HAMSTER. (E.) Arcadi, J. A. (Dept. Biol., Whittier Coll., Cal.). Science 142:592-593, 1963.

Histochemical studies were made of an estradiol-induced, estrogen dependent hamster renal tumor obtained from Kirkman, and of a transplanted estrogen-dependent and autonomous tumor originating from the same tumor (carried in diethylstilbestrol-treated male hamsters). When the tumor tissue is either lyophilized or frozen, and then substituted in absolute alcohol containing mercuric chloride, glycogen is demonstrable in cells thought to arise from the connective tissue matrix between tumor masses, and also in cells scattered within the tumor masses. The presence of glycogen in the hamster tumor increases the parameters of similarity between it and human renal tumors, and adds a possible new approach to their induction through study of intermediate pathways of glycogen metabolism.

- 64-1912 DELAYED FLUORESCENCE OF 3:4-BENZOPYRENE SOLUTIONS. (E.) Parker, C. A. (Admiralty Materials Lab., Holton Heath, Poole,

Dorset, England). Nature (London) 200:331-332, 1963.

Studies of delayed emission spectra from 3,4-benzpyrene soln. in ethanol determined at temperatures from +54°C to -110°C suggest that there is a transition from a collisional mechanism of triplet-triplet interaction at the higher temperature through an intermediate temperature where both collisional and long-range interaction occur, to low temperature where only long-range molecular interactions are observed. Similar results are obtained with pyrene at room temperature, although the relative intensity of the delayed emission spectra of pyrene and benzpyrene exhibit peaks around -20° and -80°C, resp.

- 64-1913 COMPONENTS OF CIGARETTE SMOKE WITH CILIARY-DEPRESSANT ACTIVITY. THEIR SELECTIVE REMOVAL BY FILTERS CONTAINING ACTIVATED CHARCOAL GRANULES. (E.) Kensler, C. J. (Dept. Pharmacol., Boston U. Sch. Med., Mass.) and S. F. Battista. New Eng. J. Med. 269(22):1161-1166, 1963.

A quantitative method of studying the effect of repeated short-duration exposures to gases and aerosols on mammalian (usually rabbit) ciliary transport activity is described. The smoke of 7 different brands of commercial cigarettes (5 filter types, 2 regular) inhibited this transport activity. When particulate matter was removed from the smoke of the 2 regular brands, ciliastatic activity was about the same as for the whole smoke. Although the whole smoke of the filter cigarettes decreased the phenol content by about 80%, there was no appreciable difference in ciliary-depressant activity. One brand, which contained a carbon-impregnated filter as well as cellulose acetate, appeared to be slightly less depressant. Among the various components of the gas phase found to have appreciable ciliary-depressant activity were hydrogen cyanide, ammonia, formaldehyde, acrolein and nitrogen dioxide.

- 64-1914 RELIGHTING OF CIGARETTES AND LUNG CANCER. (E.) Dark, J. (Manchester Chest Clin., England), M. Pemberton, M. O'Connor and M. H. Russell. Brit. Med. J. 2:1164-1166, 1963.

When the smoking habits of 1,000 male smokers aged 50 and over were studied, not only was the well established association of lung cancer with heavy and prolonged cigarette smoking reflected in the group, but also the habit of relighting cigarettes appeared to carry an incremental lung-cancer hazard. Thus in those who smoked 1-14, 15-29 or 30+ cigarettes per day, the incidence for all smokers was, resp., 22% of 254, 32.4% of 490, and 46.1% of 256. The incidence of cancer in "non-relighters" was: 13.2% of 129, 26% of 265, and 41.7% of 166. Comparable incidence in "relighters (2 lightings of each cigarette)" was 31.2% of 125, 40% of 22

d 54.5% of 88. These differences relative to those who smoked 1-14 and 15-29 cigarettes daily are highly significant.

1915 SNUFF DIPPER'S CANCER. (E.)

Rosenfeld, L. (Dept. Surg., Vanderbilt Med. Ctr., Nashville, Tenn.) and J. Callaway. *J. Surg.* 106(5):840-844, 1963.

From all the records of the Vanderbilt Hospital and the private practice of the senior author, 15 cases of squamous cell carcinoma were found. These cases were divided into two groups according to site: I--the tongue and floor of the mouth and II--the gingiva and buccal area (where snuff is usually placed). In series I there were 5 cases (154 men, 71 women); in this group 21% of the women admitted to the use of tobacco snuff. (Data on men relative to snuff is not given.) In contrast there were 300 pts. where the carcinoma arose in the gingivo-buccal area, and only 125 of these were men. Of the 175 women, 143 admitted to the use of snuff over many yr.; 16 gave no indication of the use of snuff and 16 denied its use. All stages in the progressive disease may be seen; multicentric sites of origin were common. The carcinomas in the inner cheek and gingiva frequently start as leukoplakia. (See also CRA 77):#1258, 1963.)

1916 PHOTO-INDUCED FREE RADICAL REACTIONS IN THE SOLUTIONS OF SOME TARS AND HUMIC ACIDS. (E.)

Lagercrantz, C. (Dept. Med. Phys., Goteborg, Sweden) and M. Yhland. *Acta Chem. Scand.* 17(5):1299-1306, 1963.

When irradiated by visible light, the free radical content in soln. of some tars and humic acids exhibits considerable changes consisting of an apparent destruction of radicals previously present in the dark (coal tar), and of formation of new radicals. Changes in radical conc. are irreversible in coal tar and humic acid soln., but show both reversible and irreversible light-induced radical formation in soln. of wood tar, chimney soot, and tobacco smoke condensate. In two experiments using tobacco smoke condensate and chimney soot the yield of free radicals on irradiation was increased considerably by the addition of ascorbic acid. On the basis of these data it is tentatively proposed that a photo-induced charge transfer reaction occurs between aromatic substances and colored acceptor substances, with the darker pigments of some of the substances acting as the acceptors.

1917 EXPERIMENTAL INDUCTION OF GLIOGENOUS TUMORS IN RATS. A HISTOPATHOLOGIC AND ELECTRON MICROSCOPE STUDY. (E.)

Ishida, Y. (Dept. Path., Gunma U. Sch. Med., Maebashi, Japan), Kawai, K. Sato and H. Niibe. *Gunma J. Med.* 12(1):36-72, 1963.

After the intracranial implantation of 20-methyl-cholanthrene, no tumors developed in 54 Wistar rats. Among 158 Donryu strain rats, tumor incidence was: gliomas 13, mixed glioma and sarcoma 1, meningiomas 2, sarcomas 4, epidermoid tumor 1, 2 granulomas and 1 unclassified. Upon further classification of the gliomas (applying criteria employed in the classification of human gliomas) 7 were glioblastomas, 3 oligodendrogliomas, 2 astrocytoma-like tumors, and 1 an ependymoma-like tumor. The experimental tumors were more mixed in character than equivalent human tumors. Typical formation of whorls was seen in the 2 meningiomas. Six tumors (4 gliomas, 1 meningioma and 1 sarcoma) were successfully transplanted into the brain, peritoneal cavity and in some cases the anterior chamber of the eye. Electron microscopy of some of the tumors reflected the very mixed structural character seen with the light microscope.

64-1918 SERUM OPTICAL ROTATION DURING THE DEVELOPMENT OF RAT-LIVER TUMOURS INDUCED BY FEEDING 4-DIMETHYLAMINOAZOBENZENE. (E.)

Fare, G. (Dept. Path., U. Birmingham Sch. Med., England). *Nature (London)* 200:481-482, 1963.

When female rats were fed 4-dimethylaminoazobenzene (DAB; 0.09%) in a corn (maize; M) diet, all developed liver tumors after an av. latent period of 8.5 mo. When 0.5% cupric oxyacetate hexahydrate (Cu) was added, a good degree of protection was given and no tumor was found after treatment for up to 500 days. Mean serum levorotatory optical rotation (x100) after 50-500 days for dietary groups M, M + DAB, and M + DAB + Cu were, resp., 46.2, 43.1 and 39.0. Differences between all groups were significant. In small scale experiments it was found that copper acetate alone (which caused no liver damage) gave as great a fall in optical rotation as the dye alone. Thioacetamide, which caused cholangiofibrosis, gave only a small drop in serum rotation. With thioacetamide + copper acetate there was only slight damage and a fall in rotation intermediate between those obtained with DAB and DAB + copper.

64-1919 CARCINOGENIC ACTIVITY OF SOME FLUORINATED POLYCYCLICS. (E.)

Bergmann, E. D. (Dept. Org. Chem., Hebrew U., Jerusalem, Israel), J. Blum and A. Haddow. *Nature (London)* 200:480, 1963.

The fluorinated derivative 3-fluoro-6,10-dimethyl-1,2-benzacridine was found to be only slightly carcinogenic; the 3-fluoro-7,10- derivative was more markedly carcinogenic. In the Walker inhibition test these 2 benzacridines as well as 3-fluoro-9-methyl- and 3-fluoro-9,10-dimethyl-1,2-benzanthracene have proved active. In view of the approx. equal carcinogenicity of 9-methyl-, 10-methyl- and 9,10-dimethyl-1,2-benzanthracene, the very high activity of 3-fluoro-9-methyl-1,2-benzanthracene is unexpected.

- 64-1920 EXPERIMENTAL STUDIES OF THE EFFECTS OF PASSIVE INHALATION OF CIGARETTE SMOKE IN MICE. (Ger.) Otto, H. (Inst. Path. Anat., U. Erlangen-Nürnberg, Germany). Frankfurt Zschr. Path. 73(1):10-23, 1963.

Inbred albino mice were brought daily to the limits of physiological tolerance (i.e. maximal exposure without anorexia or apathy) via passive inhalation of the smoke from 12 cigarettes for periods of 60-90 min./day for 2.5-25 mo. The incidence of cancers was as follows: mammary carcinoma, 6/219; renal carcinoma, 1/219; pulmonary basal cell carcinoma, 2/219; hepatic carcinoma concurrent with a salivary gland carcinoma of alveolar structure, 1/219; pulmonary adenomas in 21/219 (including 11 in a single group of 30 mice treated for 24 mo.). Among controls not exposed to smoke, the spontaneous incidence of cancers was: mammary carcinomas (part solid and part glandular), 5/60; adenoid-cystic-basal-carcinoma type skin tumors, 3/60; pulmonary adenomas, 3/60. Varying degrees of adenomatiform epithelial differentiation, especially in the region of the bronchi terminales, were seen in most of the treated animals, although increased epithelial proliferation in aging rats was approx. equal in the control and treated groups. Treated animals also showed "smoker's cells" (i.e., large, exfoliative, superficial alveolar cells which frequently had small, pyknotic nuclei and yellow-brownish cytoplasm). Among 30 mice receiving 0.5 ml saturated soln. 3,4-benzpyrene (BP) i.p. prior to 19.5 mo. exposure to the smoke of 12 cigarettes for 90 min./day, 1 case each developed mammary carcinoma, extensively metastasized hepatic carcinoma, non-metastasized hepatic carcinoma, basal cell carcinoma of the forestomach and papilloma of the forestomach; 6/30 developed multiple pulmonary adenomas. Among controls receiving BP alone, 2/30 developed hepatic carcinomas; 1/30, papilloma of the forestomach; 1/30, pulmonary adenoma (within 11 mo.).

- 64-1921 STUDY OF 20-METHYL CHOLANTHRENE INDUCED TUMOURS IN MICE. (E.) Rao, P. S. and D. J. Reddy. Indian J. Surg. 25(9):672-683, 1963.

20-Methylcholanthrene (20-Me; 1.75 mg) combined with beeswax was impregnated into lengths of string and fixed in the cervical canal of 23 inbred female virgin Swiss mice at an av. age of 197.6 days; av. survival was 205 days. Among 13 mice autopsied, besides 6 with epitheliomas of the uterine cervix, the following extra uterine tumors were seen: 2 breast adenocarcinomas, 1 reticulum cell sarcoma of the spleen (concomitant with cervical carcinoma), 1 sarcoma of the retroperitoneal tissues, and 1 hepatoma. One mouse had a tumor of the ovary, carcinoma of the cervix and a hepatoma. In 2 mice the string slipped out of the cervix and induced epitheliomas of the skin. Among 11 autopsied control mice where beeswax alone was used to impregnate the string, 1

adenocarcinoma of the breast was found.

- 64-1922 A NEW METHOD OF PRODUCING ENDOMETRIAL CANCER IN MICE. (E.) Taki, I. (Dept. Obstet. Gynec., Osaka U. Sch. Med., Japan) and H. Iijima. Am. J. Obstet. Gynec. 87(7):926-934, 1963.

This appears to be an extension of work reported as CRA 1(9-10):#1679, 1964 on the effect of 20-methylcholanthrene-impregnated threads fixed with in the uterine horns of 110 adult virgin mice. During a period of 18 wk. 32 developed adenocarcinomas (1 with a squamous cell carcinoma); 2 developed squamous cell carcinoma alone. Other changes of the endometrium included hyperplasia (9), atypical hyperplasia (58) and metaplastic change (14). With reference to changes of the endometrial stroma, 2 sarcomas were found, as well as 4 squamous cell carcinomas (2 in the columnar area of the lower uterine horn and cervix, 2 in the squamous area of the cervix). Fibrosis was found in 97 cases, and inflammatory change in 98. There were 3 cases of adenoacanthoma. At autopsy the thread was found to have slipped out in 4 cases.

- 64-1923 CORRELATION BETWEEN THE STRUCTURAL FEATURES OF INDUCED SALIVARY GLAND TUMORS AND THEIR INNERVATION. (E.) Skorodumova, I. V. (Inst. Norm. Pathol. Physiol., Acad. Med. Sci., Moscow). Bull. Expl. Biol. Med. 54(10):1157-1160, 1963.

9,10-Dimethyl-1,2-benzanthracene (5 mg in 0.1 ml of liquid petrolatum) was inj. into the right submandibular salivary gland of 40 mongrel albino rats. During the next 1.5 yr., 17 developed neoplasms. Nerve structures were found in 9/11 tumors of connective tissue origin (1 histiocytoma, 1/2 lymphosarcomas, 2 fibrosarcomas and 5/6 spindle cell sarcomas). All 6 tumors of epithelial origin (3 adenoma, 1 each epithelioma of the salivary gland, mixed salivary gland tumor, squamous cell carcinoma) showed intact nervous structures. The innervation of the morphologically more mature tumors (mastocytoma, fibrosarcoma) showed little or no change from the normal. In the histiocytoma (reticulosarcoma) and in the sarcomas the nerve trunks showed evidences of chronic irritation (hyperargyrophilia, changes in the caliber and varicosities of the nerve fibers). Benign neoplasms (such as the mixed tumor of the salivary gland) showed the most differentiated receptors with profuse arborization as well as polyvalent receptors.

- 64-1924 STUDY OF BERYLLIUM-INDUCED OSTEOGENIC SARCOMA. (Jap.) Yamaguchi, S. (Dept. Orthoped., Nagasaki U. Sch. Med., Japan). Nagasaki Igakkai Zasshi (Nagasaki Med. J.) 38(2):127-138, 1963.

1 inj. of BeO (beryllium oxide) into the shaft of the femur produced osteochondrosarcoma, osteosarcoma or presarcomatous changes in 84% of young rats. The highest incidence was obtained after 10 inj., each 20 mg. The av. latent period (from the final inj. to development of tumor) was 180 days. Metastases usually occurred in the liver, kidney, lymph nodes and most frequently in the lungs.

925 EFFECTS OF p-DIMETHYLAMINOAZOBENZENE ON THE FINE STRUCTURE OF RAT LIVER CELLS.

Timme, A. H. (Dept. Path., U. Cape Town Med., S. Afr.) and L. G. Fowle. Nature (London) 200:694-695, 1963.

After feeding albino male rats with p-dimethylaminoazobenzene (1% in corn) for 7 mo. (at which time some had developed hepatocellular and cholangiocarcinomas) non-neoplastic tissue in perivascular areas was studied. It was found that the plasma membrane had been transformed into a convoluted mass of vesicles of varying sizes; it did not contain any electron-dense material and was clearly delimited by smooth cytoplasmic membranes. At random points the membranes were densely crowded, and here varying stages of vesicle formation were evident. These whorls consisted of circularly arranged paired membranes surrounding an inner zone which contained faintly electron-dense material or poorly outlined membranes. Although most mitochondria were normal, some were irregularly shaped, others were swollen, and some possessed inconspicuous cristae. The changes observed in the endoplasmic reticulum appeared similar to those following admin. of thionin, thioamide, dimethylnitrosamine and ethionine.

926 CANCERIZATION OF THE LIVER OF RATS BY DIMETHYLAMINOAZOBENZENE (DAB). INFLUENCE OF STRAIN AND NUTRITIONAL FACTORS ON THE EFFECTS OF ADRENALECTOMY AND CORTISONE. (Fr.) Chany, E. (Cell Physiol. Lab., C.N.R.S., Villejuif, Seine, France), G. Broy and E. Le Breton. Arch. Sci. Physiol. 15:327-344, 1963.

Dimethylaminoazobenzene (DAB)-induced hepatomas were produced at different rates depending on whether the agent was admin. in a protein deficient or adequate diet. In Wag strain rats, the differences were not significant (6-10 mo. with deficient diet; 5-9 mo. with an adequate diet), but in Commentry strain rats, the animals receiving the deficient diet developed the tumors earlier (9-12 mo.) than those on the adequate diets (15-21 mo.). The addition of cortisone (125 mg/kg; route not stated) or triamcinolone (4 mg/kg; route not stated) to the deficient diet speeded up the appearance of the tumors in Wag strain (3-4 mo.); the addition of cortisone (triamcinolone not assayed) had a similar effect in Commentry rats (4-7 mo.). The drugs did not change the time of tumor onset in animals

of both strains which received the adequate diet. The addition of corticoids to a deficient diet also changed the nature of the tumor from a classical hepatoma to a tumor with a sclerotic stromal reaction. In the Wag strain only their addition to an adequate diet produced similar effects. In females of the Commentry strain, adrenalectomized and maintained on the deficient diet, the operation did not bring about the beneficial results previously observed when the diet was adequate for protein.

64-1927 DETECTION OF A METABOLIC PARAMETER OF CARCINOGENESIS IN THE SERUM OF RATS FED DIMETHYLAMINOAZOBENZENE. (Fr.) Dufour, D. (Dept. Biochem., U. Laval, Quebec, Canada) and J.-M. Boucher. Bull. Assn. Franc. Cancer 50(2):305-308, 1963.

Sprague-Dawley rats fed dimethylaminoazobenzene (DAB) for 2, 4, or 6 mo. (no details) showed apparently increased electrophoretic mobility of the serum albumin and α_1 -globulin fractions, and also a new globulin fraction with a mobility intermediate between normal β and α_1' . The presence of a new serum fraction was confirmed by immunoelectrophoresis, but the component was identified as a new protein partially associated with albumin.

64-1928 SPECTROSCOPIC ANALYSIS OF CARCINOGENIC HYDROCARBONS IN BIOLOGICAL INTERACTION IN VIVO AND IN VITRO. (E.) Sloane, G. H. I. (Dept. Anat., Western Res. U., Cleveland, Ohio) and C. N. Loeser. Cancer Res. 23(9):1555-1565, 1963.

After implantation of 3,4-benzpyrene (BP) in the rabbit ear chamber, in vivo fluorescence spectroscopy revealed various carcinogen-tissue complexes. A uniform spectrum was always obtained anywhere in the chamber immediately after implantation; its form suggests an initial soln. of BP similar to that produced in serum. Within 1-22 days, emission spectra (which appeared to originate intracellularly) were obtained similar to those of metabolites isolated through in vitro procedures as previously reported. The intensity of fluorescence was greatest shortly after implantation and decreased as a function of time. 20-Methylcholanthrene in the ear chamber and 1,2,5,6-dibenzanthracene in the exposed lung (rabbit and rat) underwent spectral alteration much more slowly than when BP was similarly implanted. In vitro experiments with microcrystals of carcinogen and ascites cells revealed spectra similar to those produced early after implantation in the ear chamber. Fluorescence emission spectra of BP in polar and nonpolar solvents and in serum were similar. Rate of soln. of BP in serum was characterized by different slopes for each emission max. The spectrally demonstrable serum interactions of the various hydrocarbons studied were not specific for those that were carcinogens.

64-1929 ANTHRAMINE CARCINOGENESIS IN THE SKIN OF RATS. I. THE EPIDERMIS. (E.)

Dobson, R. L. (Div. Derm., U. Oregon Sch. Med., Portland). J. Nat. Cancer Inst. 31(4):841-859, 1963.

In a 36-wk. study, the interscapular area of 108 male albino Carworth Farms rats was painted twice weekly with about 0.15 ml of a 1% 2-anthramine soln. in acetone. One treated rat was killed weekly for study and compared with acetone-treated and untreated controls. Both basal cell epitheliomas and some squamous cell carcinomas developed, both from the stratum germinativum of the epidermis. The evolution of the basal cell tumors appeared consistently correlated with the condition of the underlying dermis. If the basement membrane of the epidermis was intact, only intraepidermal tumors resulted. With disruption of the basement membrane, downward proliferation of nests of basal cells occurred. Proliferation progressed until normal connective tissue was encountered. Organized stromal elements formed in relation to the epithelial masses which differentiated, forming a caricature of the pilary apparatus. The squamous cell epithelioma, did not appear to participate in such a relationship. The difference in the malignant potentialities of basal and squamous cell epitheliomas may reflect the response or lack of response of these tumors to factors associated with connective tissue.

64-1930 ANTHRAMINE CARCINOGENESIS IN THE SKIN OF RATS. II. THE PILOSEBACEOUS APPARATUS. (E.) Dobson, R. L. (Div. Derm., U. Oregon Sch. Med., Portland). J. Nat. Cancer Inst. 31(4):861-871, 1963.

Repeated application of 2-anthramine to the skin of rats resulted in the formation of undifferentiated nests of basal cells derived from hair follicles. Basal cell epitheliomas arising from these nests proliferated only if the surrounding connective tissue was abnormal. Eventually, tumors resulted, with both epithelial and stromal components resembling a part or parts of the hair follicle. Cells derived from the hair follicle also produced squamous cell carcinomas. Similar nests of cells arose from sebaceous glands, but these cells appeared incapable of hair-follicle differentiation, although sebaceous gland tumors, undifferentiated basal cell epitheliomas, and squamous cell carcinomas were seen. The results suggest stromal control over the growth of cells derived from hair follicles. Sebaceous gland cells derived from a localized area of the hair follicle appeared to have inherent control and thus could not produce follicle-like structures under the influence of connective-tissue organizers. (See also CRA 1(11):#1929, 1964.)

64-1931 CARCINOGENIC PROPERTIES OF NUTS FROM CYCAS CIRCINALIS L. INDIGENOUS TO GUAM. Laqueur, G. L. (Natl. Inst. Arthritis Metabolic

Dis., Bethesda, Md.), O. Mickelsen, M. G. Whit and L. T. Kurland. J. Nat. Cancer Inst. 31(4):919-951, 1963.

As part of a search originally for substances containing a neurotoxin, flour prepared from the cad nut was fed to rats in amounts from 1-3% of the diet. After 6-9 mo. there developed a number of benign and malignant tumors, mainly in the liver and kidneys with 1 in the lung and 2 in the testine. The undifferentiated tumors of the kidney were thought to have originated from cells between tubules and capillaries in the inner cortex and grew infiltratively between pre-existing renal structures. There are definite similarities in the pathologic changes between rats fed toxic cycad nut meal and those, reported in the literature, given dimethylnitrosamine. The possibility exists that a glycoside isolated from cycads, namely cycasin, may yield in its metabolic breakdown a compound carcinogenic for rats and similar to the one suggested as the carcinogenic agent, dimethylnitrosamine.

64-1932 TUMOR PROGRESSION IN TWO MAMMARY CARCINOMAS OF THE RAT INDUCED BY ACETYLAMINOFLUORENE. (Fr.) Van den Berghe, H. (Vesalius Inst., Morph. Lab., Louvain, Belgium) and H. Verresen. Bull. Assn. Franc. Cancer 50(2):291-303, 1963.

Two mammary tumors, DE 40 (a papillary adenocarcinoma), and DE 7 (a well-differentiated adenocarcinoma with massive tubular glandular structures) were found in R strain rats fed 2-acetylaminofluorene. Their behavior on subsequent transplantation into R strain females was studied in detail. In the DE 7 tumor autonomy developed abruptly on the second passage, whereas in the DE 40 tumor autonomy appeared gradually during the course of 20 subpassages. Autonomy was characterized by increased virulence, sarcomatoid transformation, and disappearance of hormone-dependence. The latter could be accelerated by transplantation into male R strain rats. Although the 3 changes are thought to be linked, dissociation could be obtained on some subpassages in male animals, where sarcomatoid transformation was accompanied by low virulence. Culture in vivo of sarcomatoid tumors showed that the basic nature of the cells remained epithelial.

64-1933 EXPERIMENTAL STUDIES ON THE HISTOGENESIS OF MENINGEAL SARCOMA AND INTRACEREBRAL TRANSPLANTATION OF TUMOR. (Jap.) Totsuka, S. (Dept. Neuropsychiatry, Chiba U. Sch. Med., Japan). J. Chiba Med. Soc. (Chiba Igakkai Zasshi) 39(1):10-22, 1963.

When crystals of 20-methylcholanthrene were implanted into the left parietal areas of the brain of 73 hybrid mice, meningeal sarcomas developed in 11. Survival time after implantation ranged from 121-238 days. As to histological type, 2

e polymorphous, 2 spindle cell and 7 fibrocomas. The polymorphous type was the most immature and malignant, not only on the basis of histologic structure but also because of an increase in intracellular RNA and DNA. It was concluded that the induced tumors were derived from primitive meningeal mesenchyme.

1934 FAILURE OF MONO-CHLOROACETONE TO INFLUENCE 3,4-BENZOPYRENE MOUSE SKIN TUMOR GENESIS. (E.) Argus, M. F. (Seamen's Mem. Lab., USPHS Hosp., New Orleans, La.) and J. Arcos. *Experientia* 19(11):588-589, 1963.

groups of random bred Swiss Webster mice received topically on the interscapular skin 3,4-benzopyrene (BP; 0.1 ml of a 0.3% soln. in benzene) and/or monochloroacetone (CA; 0.1 ml of a 0.1% soln. from 0.1-4.0%) 3x/wk. (on different days). After 18 wk. treatment, while the previously described high incidence of tumors with BP alone was confirmed, there was no inhibition of tumor growth combined with CA in any of the conc. used.

1935 EXPERIMENTAL INVESTIGATION ON CARCINOGENESIS OF THE GALLBLADDER WITH 3,4-BENZOPYRENE. (It.) Rovati, L. (Inst. Gen. Surg. and Surg. Therap., U. Pavia, Italy), G. Ragaglia, F. De Luca. *Riv. Pat. Clin.* 18(5):227-233, 1963.

30 days following the inj. of 3,4-benzopyrene (15 mg in 0.5 ml of olive oil) into the wall of the gallbladder of rabbits there was some reaction of the gallbladder with signs of pericholecystitis. There were no apparent changes in the epithelium and only a slight thickening of the muscle and serous layers. Thirty days later the organ was further retracted and showed intense pericholecystitis. The lining epithelium was no longer in a single layer and had lost its cuboidal shape. By 180 days following inj. of BP the gallbladder was greatly retracted and covered with adhesions. All the papillae were flattened, the epithelium was thickened and multi-layered with small cells with prominent basophilic cytoplasm. The muscle and serous layers were thickened and showed infiltration by round cell elements. Controls receiving only the oily vehicle showed only signs of pericholecystitis.

1936 HISTOLOGICAL AND ENZYMATIC CHANGES IN THE LIVERS OF RATS FED THE HEPATIC CARCINOGEN DIETHYLNITROSAMINE. (E.) Reid, J. D. (Pharm., Queen's Coll., U. St. Andrews, Scotland), J. F. Riley and D. M. Shepherd. *Chem. Pharmacol.* 12(10):1151-1156, 1963.

Diethylnitrosamine was fed to Wistar rats in their drinking water (1.5 mg/rat daily) for a period of up to 5 mo. two main changes were observed to appear in the liver. At first (about

2 wk.) the hepatic cells showed cloudy swelling, vacuolization and patchy necrosis. Around 3.5-4 mo. nodular hepatomas appeared, some of which were visible to the naked eye. As the hepatomas increased in size there occurred a rapid proliferation of bile duct elements which terminated in the formation of cholangiomas with later death of the animals due to depressed liver function. Specific (pH 6.5) histidine decarboxylase increased in the liver in association with the hepatoma formation. In addition, in both control and carcinogen-treated animals a significant positive correlation was observed between the histidine decarboxylase activity at pH 8.0 and the dihydroxyphenylalanine and 5-hydroxytryptophan decarboxylase activities. The authors suggest that these 3 activities are due to a single enzyme.

64-1937 EFFECT OF α -TOCOPHERYL ACETATE ON LIVER GLUTATHIONE OF MALE RATS INJECTED WITH 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE. (E.) Neish, W. J. P. (Cancer Res. Unit, U. Sheffield, England) and A. Rylett. *Biochem. Pharmacol.* 12(10):1147-1150, 1963.

The increase in glutathione observed in the livers of albino rats following the admin. of 3'-methyl-4-dimethylaminoazobenzene (16.3 mg/100 g i.p.) was constantly decreased 14-15% by the simultaneous admin. of 20 or 100 mg of D or DL- α -tocopheryl acetate. The stomach dilation which was observed 24 hr. after the inj. of the carcinogen was inhibited by 20 mg but not 100 mg of the D- α -tocopheryl acetate and by 100 but not 20 or 200 mg of the DL mixture.

64-1938 CARCINOGENIC ACTION OF PRONETHALOL. (E., Abstract) Paget, G. E. (Imperial Chem. Industries Ltd., Macclesfield, Cheshire, England). *Brit. Med. J.* 2:1266-1267, 1963.

Pronethalol (Alderlin) admin. in doses of up to 200 mg/kg for periods of up to 2 yr. to rats and to dogs for up to 1 yr. did not produce any significant tissue changes. When similar experiments were carried out in mice, tumors were formed, principally in the thymus beginning at about 3 mo. after initiation of admin. The total number was related to the dose admin. As the experiments progressed there developed generalized lymphosarcomas, unusual reticulosarcomas of the liver, spleen and genital tract. Tumors of other systems were not seen more frequently than in controls.

64-1939 WATER-SOLUBLE PRODUCTS OF METHYL CHOLANTHRENE AND THEIR EFFECT ON BACTERIAL GROWTH. (E.) Johnson, G. T. (Dept. Bot., U. Arkansas, Fayetteville). *Nature (London)* 200:805-806, 1963.

Methylcholanthrene (62.5-500 μ g/ml) dissolved in the oil layer above the hydrocarbon nutrient medium for *Bacterium aliphaticum* adversely affected

the population size and long term viability of cultures. After 4 yr. storage ($28^{\circ} \pm 2^{\circ}\text{C}$) 47% of the cultures containing the carcinogen had expired; no control cultures died. By 7 and 10 yr. the expired proportion, resp., was 70 and 100% (7 and 15% in controls). The frequency of death of cultures was roughly proportional to the dose of agent. During the first 10 wk. of incub. there appeared a distinct fluorescence in the water layer of the cultures. Chromatographic analysis and purification of the fluorescing product showed it to be different from methylcholanthrene and slightly inhibitory to both Bacillus subtilis and Staphylococcus aureus.

64-1940 THE EFFECT OF CYCLOPHOSPHAMIDE ON 2-AMINOANTHRACENE CARCINOGENESIS IN RAT SKIN. (E.) Dobson, R. L. (Div. Derm., U. Oregon Sch. Med., Portland). J. Invest. Derm. 41(6): 475-477, 1963.

Male albino rats were painted 2x/wk. on the skin of the back with 2-aminoanthracene (1% in acetone). Three starting groups of 12 each were additionally treated with i.p. inj. cyclophosphamide in 0.85% saline 2x/wk.: Group I, 0.1 mg; Group II, 0.25 mg; Group III, 0.5 mg, resp. A fourth group of 80 (controls) received the carcinogen only. Among survivors, the approx. incidence of squamous cell carcinomas was Group I 70% of 10; Group II 82% of 11; controls 38% of 76. Incidence of sebaceous gland carcinoma was Group I 30%, Group II 28%, controls 10%; of fibrosarcoma Group I 40%, Group II 20%, controls 60%; of basal cell carcinoma Group I 80%, Group II 90%, controls 92%. It could not be determined whether the cyclophosphamide prevented the development of fibrosarcomas or destroyed them after their development.

64-1941 A CLONAL SELECTION THEORY OF CHEMICAL CARCINOGENESIS. (E.) Prehn, R. T. (Dept. Path., U. Washington, Seattle). J. Nat. Cancer Inst. 32(1):1-17, 1964.

An attempt was made to describe a possible mechanism of clonal selection during chemical carcinogenesis. The mechanism, based on a differential toxicity of a carcinogen with respect to normal and malignant cells, appears consistent with the currently known phenomena of carcinogenesis. It seems to account for some of these phenomena in a somewhat easier fashion than has been done here-

tofore. The theory, as formulated, cannot be described as entirely new, but is rather a modulation and synthesis of previous theories, which it modifies or restates. This clonal selection theory gives rise to some testable predictions, among which are the following: 1) All chemical carcinogens will display, either directly or indirectly, a greater toxicity for normal tissue cells than for the cells of a tumor derived therefrom by treatment with that carcinogen. 2) All agents displaying a greater toxicity (i.e., capacity to interfere with cellular reproduction) for normal tissue cells than for tumor cells will be carcinogens. (See also CRA 1(11):#1859, 1964)

64-1942 METHYLATION OF RIBONUCLEIC ACIDS OF LIVER AND OTHER ORGANS IN DIFFERENT SPECIES TREATED WITH C^{14} - AND H^3 -DIMETHYLNITROSAMINES IN VIVO. (E.) Lee, K. Y. (Div. Oncol., Chicago Sch. Med., Ill.), W. Lijinsky and P. N. Magee. J. Nat. Cancer Inst. 32(1):65-76, 1964.

When the carcinogen dimethylnitrosamine (DMN), labeled with radioactive carbon (C^{14} -DMN), was inj. into rats, mice, hamsters, and guinea pigs in doses sufficient to cause acute hepatic necrosis, radioactivity was found in the RNA of liver, kidney, spleen, and pancreas. Incorporation was greatest in liver and least in pancreas, with intermediate values in kidney and spleen that showed some species differences. Ion-exchange chromatographic profiles of hydrolysates of the labeled liver RNA's confirmed previous work with the rat and showed similar patterns in the other species, which indicated that most of the radioactivity was present as 7-methylguanine and suggested that methylation of the RNA's had occurred in vivo. Tritiated DMN (H^3 -DMN) was prepared by the Wilzbach exchange reaction, and its metabolic fate was compared with that of C^{14} -DMN in rats and mice. The tritium was also incorporated into the RNA's of liver and other organs in both species, the distribution showing some similarities to and some dissimilarities to that observed with C^{14} -DMN. Comparison of the ion-exchange chromatographic profiles of hydrolysates of the labeled RNA's from different organs confirmed that incorporation probably occurs by two processes: (1) via normal "carbon" metabolic intermediates; (2) by methylation of the nucleic acids. In both rat and mouse the liver showed the highest degree of methylation, with the next highest in the kidney of the rat and lung of the mouse; the other organs showed low values.

See also abstract nos.: 1859, 1869, 1871, 1873, 1877, 1881

VIRAL CARCINOGENESIS

1943 SEARCH FOR ONCOGENIC PROPERTIES IN
VARIOUS VIRUSES FOUND IN MAN: POSITIVE
RESULTS WITH ADENOVIRUS TYPES 12 AND 18. (E.)
Leod, D. L. (Div. Biol. Res., Ontario Cancer
Inst., Toronto, Canada) and A. W. Ham. Canad.
J. Assn. J. 89(16):799-805, 1963.

or trials in newborn Syrian hamsters are
cribed for various viruses: Polio I and II;
Sackie A9, A16 and A21; Echo 9, parainfluenza
; Vaccinia (IHD); Varicella Zoster; Rubeola;
no 3, 12 (Huie) and 18 (D.C.); Canine Adeno
161. In all, 25 experiments were performed,
ng in most cases at least 2 different routes
Inj. After intrathoracic (i.t.) inj. of Adeno
tumor incidence in 2 experiments was 12/42
2/19 of those that survived over 3 wk.; after
inj., tumors occurred in 27/31 and 15/30.
er i.t. inj. of Adeno 18, tumor incidence
15/67.

1944 THE ONCOGENIC ACTIVITY OF THE POLYOMA
VIRUS IN THYMECTOMIZED RATS. (E.)
deputte, M. (Rega Inst., U. Louvain, Belgium),
Denys, Jr., R. Leyten and P. de Somer. Life
7:475-478, 1963.

a further report of work previously reported
e CRA 1(8):#1566, 1963), Albino R strain rats
e thymectomized within the first 18 hr. after
th and then inj. s.c. with polyoma virus
7 TCID₅₀). At the end of 3 mo. the incidence
sarcoma (kidney) was 86% (18/21) in virus-
ated rats compared to 21% (3/14) in sham-
rated and 13/42 in nonoperated rats (including
liposarcoma). In the 18 virus-treated rats
n tumors, 2 also had liposarcomas and 1 an
osarcoma. High hemagglutination-inhibition
body titers (1/4,000-1/32,000) were found in
ually all tumor-bearing rats. No difference
iter was recorded between thymectomized and
control rats.

1945 ISOLATION OF A LATENT VIRUS FROM THE
KIDNEY OF A NEWBORN HUMAN. (E., Abstract)
hardt, F. and A. W. Holmes. J. Lab. Clin.
62(5):872, 1963.

rus has been recovered from a "normal" human
ey obtained from a prematurely born child
h had multiple malformations. The virus
plies slowly in a variety of tissue cultures;
b. periods of up to 28 days are required to
h titration end points. The virus induces
formation of large syncytia. No inclusion
es have been demonstrated in infected cul-
s, but with acridine-orange stains intensely
n-staining intranuclear globules are observed
in the infectious process. In a preliminary
riment the virus was inhibited by 5-iodo-2'-
yridine, which may indicate that this is a
virus. The mother had no illnesses during

the pregnancy and has 4 healthy children. The
father has suffered for 3 yr. from recurrent
multiple carcinoma of the upper respiratory tract.

64-1946 SOME PROBLEMS OF THE EARLY STAGES OF
LEUKEMIA. (Pol.) Ambs, E. (Dept.
Path., Karolinska Inst., Stockholm, Sweden) and
B. Thorell. Pediat. Pol. 38(7):609-618, 1963.

A review (40 references) and discussion is pre-
sented, along with some of the authors' own work,
on vague clinical syndromes involving the erythro-
poietic system which may precede leukemia but in
which for some time no leukemic cells are found
in the bone marrow, blood, spleen or lymph nodes.
On the basis of some experimental work on the
histogenesis and cytogenesis of the early phase
of virus-induced erythroleukemia in the fowl, it
is suggested that without making an analogy to
acute leukemia in man, and while taking into
account the different etiology, the results ob-
tained could form a pattern for useful investiga-
tions in the human. (See also CRA 1(4):#612,
1963.)

64-1947 DECREASED ANTIBODY-PRODUCING CAPACITY
IN MICE DURING THE INCUBATION PERIOD
OF PASSAGE A LYMPHATIC LEUKEMIA. (E., Abstract)
Good, R. A., R. L. Vernier and R. D. A. Peterson.
J. Lab. Clin. Med. 62(5):878, 1963.

When C3Hf/Bi mice are infected i.p. at 3 days of
age with Gross passage A virus, they remain clini-
cally well until an acute lymphatic leukemia
develops in almost all of them at about 3 mo. of
age. When these mice at 3 and 9 wk. of age were
stimulated with an i.p. inj. of T2 bacteriophage
and the serum was assayed by a plaque-neutraliza-
tion technic after 2 wk., significantly less anti-
body was produced by the infected mice than by
noninfected mice.

64-1948 A SUBCELLULAR TRANSMISSIBLE AGENT FROM
EHRlich CARCINOMA CELLS PRODUCING
ASCITES TUMORS IN MICE. (E.) Tolnai, S. (Dept.
Histol. Embryol., U. Ottawa, Canada), R. Scantland
and J. F. Morgan. Canad. Cancer Conf. 5:175-189,
1963.

In a detailed study of the relationship between
centrifugation speeds and distribution of tumor-
inducing capacity, it was found that both the
supernatant and sediment of Ehrlich ascites fluid
from cultures subjected to 40,000 rpm for 1 hr.
was active in inducing tumors when inoc. into mice.
The activity of the supernatant, was, however,
lost when subjected to filtration through various
filters. Dilution of the supernatant 1:2560 still
produced 100% tumors upon inj. of 0.25 ml/mouse.
Further evidence for a subcellular agent is the
increase in virulence seen with passage. When

chromosome analyses were made of the tumor cells in mice, those which resulted from inj. with intact ascites cells showed 2 pairs of marker chromosomes, while tumor cells of mice inj. with the supernatant showed 5 and 6 pairs of marker chromosomes.

64-1949 SEASONAL VARIATION IN LEUKAEMIA INCIDENCE. (E.) Swan, A. (St. James Hosp., London S. W. 12). Brit. Med. J. 2:1063-1064, 1963.

After comment on a previous report of bimodal seasonal variation in leukemia incidence, a personal series of 56 cases of acute adult leukemia is presented. The existence of two peaks (one in winter and another in spring) was noted whether the time of clinical onset was studied, or the moment of diagnosis, or that of death. It is commented that the bimodal seasonal variation of certain types of leukemia may be fruitfully compared with that of other neoplastic diseases and diseases of viral etiology.

64-1950 RESPONSE OF GERM-FREE MICE TO FRIEND VIRUS. (E.) Mirand, E. A. (Roswell Park Mem. Inst., Buffalo, N. Y.) and J. T. Grace, Jr. Nature (London) 200:92-93, 1963.

A comparison of early changes in Hauschka-Mirand/ICR Swiss mice infected with Friend's virus (0.2 ml cell-free filtrate from infected spleens, i.p.) at age 7 wk. revealed that at 14 and 21 days after infection (but not at 7 days) response was greater in germ-free animals than in conventionalized (germ-free exposed to open-animal-room feces) or open-animal-room reared mice. However, positive responses were observed in all groups, and included a rise in spleen wt., in hematocrit, WBC, and RBC. The latter was accompanied by erythroblasts in the peripheral blood and by an increase in blood volume. Although there were significant quantitative differences between changes in germ-free and control mice, the general pattern of the disease was identical in all groups. Liver wt. of germ-free animals were generally smaller than those of controls. Study of erythropoietic activity by 24 hr. Fe^{59} uptake of spleens of 14-day-infected mice gave the following uptake (per cent) for virus infected and uninfected mice: germ-free 23.6 and 2.1; conventionalized 18.9 and 3.9; and open-room reared 8.98 and 3.5. It is suggested that germ-free animals are more susceptible to Friend's leukemia, and that the susceptibility is reflected by a decreased latent period for disease production.

64-1951 BEHAVIOR OF NONINFECTIOUS SV40 VIRAL GENOME IN HAMSTER TUMOR CELLS: INDUCTION OF SYNTHESIS OF INFECTIOUS VIRUS. (E.) Sabin, A. B. (Children's Hosp. Res. Found., U. Cincinnati Coll. Med., Ohio) and M. A. Koch. Proc. Nat. Acad. Sci. USA 50(3):407-417, 1963.

In an extension of previously reported work (see CRA 1(2):#261, 1963), it was found that SV40 infectious virus (V) was more frequently recoverable from tumors that had been transplanted for more than 4 wk. No infectious nucleic acid was found in tumor cells capable of producing complete SV40 V in susceptible Cercopithecus cells. Induction of a greater frequency of synthesis of infectious V in tumor cells has been demonstrated by 3 procedures: (1) propagation of tumor cells *in vitro* (more frequently in rolled than in stationary cultures); (2) by association of viable tumor cells with susceptible cells under certain conditions of contact; (3) by an X-ray effect or a very small proportion of the tumor cells. SV40 tumors in newborn hamsters yield a complement fixing antigen which reacts specifically only with sera of hamsters bearing SV40 tumors but not with sera of hamsters bearing polyoma tumors or Fortin fibrosarcoma No. 3 tumors. Hamsters bearing transplanted SV40 tumors for 4 wk. or longer develop complement-fixing antibody for an antigen present in BS-C-1 Cercopithecus cells infected with SV40 V, although these sera contain no neutralizing antibodies. Adult hamsters inoc. with large doses of SV40 V, which induces a specific resistance to transplantation of SV40 tumor cells, possess no antibody for the antigen in the SV40 virus-infected Cercopithecus cells.

64-1952 CULTIVATION IN HUMAN EMBRYO CELLS OF VIRAL AGENT ISOLATED FROM CASES OF HODGKIN'S DISEASE. (E.) Cajal, N. (Inst. Inframicrobiol., Rumanian Acad. Sci., Bucharest). M. Cepleanu, Y. Sorodoc, A. Schacter and V. Lotreanu. Acta. Virol. (Praha) (Eng.) 7(4):379, 1963.

The agent isolated from the lymph nodes of pts. with Hodgkin's disease and grown in embryonated hen's eggs and which was subsequently adapted to the white mouse was used in a series of attempts at adaptation to cells grown *in vitro*. The mice used originally were infected with lung tritura from mice which died of the experimental disease. Human embryo cell cultures (in a lactalbumin hydrolysate nutrient medium) were used. After 1-2 blind passages following a 5-day period of incub. at 37°C, all the strains tested produced a characteristic cytopathic effect which was transmissible in series. This effect consisted of the rounding and swelling of fibroblast cells and the appearance of multiple giant cells with numerous nuclei (8-50), distributed in a circle or spread unequally at the periphery of the cell.

64-1953 CONTRIBUTION TO THE STUDY OF FRIEND'S CELLS. (Fr.) Zajdela, F. (Nat. Inst. Hygiene, Curie Found., Paris). Bull. Assn. Fra. Cancer 49(4):351-373, 1962.

A description is presented of the changes which cells undergo when mice are infected with Friend's virus. In the spleen of inoc. mice large, high basophilic "reticular" cells were found which d

not contain non-specific esterase. They were not metallophilic, did not phagocytize India ink particles nor colloidal radioactive phosphate, nor did they contain lipophylic material.

4-1954 CRYSTALLIZATION OF SE POLYOMA VIRUS. (E.) Murakami, W. T. (Grad. Dept. Biochem., Brandeis U., Waltham, Mass.). Science 142:56-58, 1963.

The SE (Stuart and Eddy) 485 strain of polyoma virus was crystallized by either of 2 procedures which are described in detail. The crystals were rhombic dodecahedra and contained 9.1×10^7 FU/ μ g DNA. The specific infectivity values were constant throughout purification procedures from the 2 methods of crystallization. Preliminary x-ray diffraction studies by R. Langridge show "powder" pattern of about 4 rings which demands a unit cell of 400 Å or more, which is in agreement with published measures of particle diameters of polyoma virus.

4-1955 LOSS OF LEUKOCYTE INDIVIDUAL SPECIFIC ANTIGENS IN A CASE OF ACUTE LEUKEMIA. (E.) Nelken, D. (Dept. Clin. Microbiol., Hebrew U.-Hadassah Sch. Med., Jerusalem). Vox Sang. 5(5):638-640, 1963.

The antigens of the granulocytes of a female pt. were examined when she was completely normal and 1 wk. after the onset of acute myelocytic leukemia. Compared to the earlier examination 11 d. before, the latter examination showed no reaction to anti-leukocyte serum No. 8. There were no changes in the reactivity of the pts. leukocytes with other anti-leukocyte sera nor in her erythrocyte antigens.

4-1956 A COMPARATIVE STUDY OF POLYOMA AND PAPILLOMA VIRUSES. (E.) Crawford, V. (Inst. Virol. U. Glasgow, Scotland) and M. Crawford. Virology 21(2):258-263, 1963.

Polyoma, Shope rabbit papilloma, bovine papilloma, canine papilloma, and human papilloma viruses were studied by electron microscopy and by preparative density gradient centrifugation in RbCl. In electron microscopy, mixtures of the denser (full) particles showed a clear cut difference between the size of the polyoma virus (about 45 m in diameter) and that of the 4 papilloma viruses (52-55 m in diameter). Sedimentation coefficients were in agreement with these data, showing values of 238 S and 140 S for full and empty polyoma virus particles, resp., and a range of 296-300 S and of 165-172 S for full and empty Shope rabbit, canine, and human papilloma. Analytical centrifugation of the viral DNA in CsCl against DNA's of known base composition gave the following estimated percentages of guanine + cytosine content from absorption spectra: polyoma 43, Shope rabbit papilloma 47, bovine papilloma

45.5, canine papilloma 43, and human papilloma 41. The polyoma DNA showed 2 components 15 S and 21 S from pH 5 to pH 8.5. Shope rabbit papilloma also showed 2 components, 21 S and 28 S, but detectable only at pH 6.5 or above, whereas at lower pH all the DNA was at the 21 S boundary. Human papilloma virus showed a similar behavior.

64-1957 DIRECT COUNTING OF THE CAPSOMERES IN POLYOMA AND PAPILLOMA VIRUSES. (E.) Howatson, A. F. (Inst. Virol., U. Glasgow, Scotland) and L. V. Crawford. Virology 21(1):1-6, 1963.

A method is described for the determination of the number of capsomeres/particle of polyoma, rabbit papilloma, and human papilloma viruses by direct counting on electron micrographs of groups derived from capsids disintegrated during drying in the presence of phosphotungstic acid. For all 3 viruses the peak distribution was around 40, which is considered consistent with a capsomere number of 42.

64-1958 A MACROFOCUS ASSAY FOR ROUS SARCOMA VIRUS (RSV) IN CHICKEN EMBRYO CELLS. (E.) Adams, E. V. (Inst. Microbiol. Rutgers U., New Brunswick, N. J.) and V. Groupé. Virology 21(2):271-273, 1963.

A 7-day macroscopic assay for RSV in second-passage chick embryo cells cultured in tubes is described. The critical step is incub. at 40°C. The assay system is highly reproducible, and in several experiments there was a linear relationship between the number of macrofoci and the infective titer of the inoculum. Staining with neutral red increases the readability of the assay.

64-1959 GENETIC-VIRAL HYPOTHESIS IN THE PATHOGENESIS OF HEMOBLASTOSES. (Fr.) Torrioli, M. (Cancer Inst., Rome). Schweiz. Med. Wschr. 93(41):1463-1465, 1963.

When fertilized eggs are inoc. with a cell-free Seitz filtrate of human leukemic blood (no details) the embryos develop a mesenchymal tissue disease. The disease is transmissible and consists of a decrease or loss of proerythroblast formation in the endothelium of the capillaries of the embryonic adnexa (the normal site of erythroblastic activity in chick embryos), accompanied by gross infiltration of the sinusoidal mesenchyme with histoid cells and highly basophilic small erythroblasts. The embryos die after 8-14 days of incub., usually as a result of severe anemia. The results are thought to be in agreement with a viral theory of leukemogenesis, where the virus induces a mutant cellular strain which consequently causes clinical disease. Suggestive evidence that a similar phenomenon occurs in human leukemias is given by a shift toward smaller peripheral lymphocyte diameters in lymphatic leukemias and lymphosarcomatosis.

- 64-1960 EVIDENCE OF MURINE, VIRUS-INDUCED, PARAPROTEIN-PRODUCING LEUKAEMIA AND ITS RELATION TO OTHER VIRUS-INDUCED LEUKAEMIAS. (E.) Rask-Nielsen, R. (Dept. Biochem., U. Copenhagen, Denmark). Nature (London) 200: 440 and 453, 1963.

Minced mammary tissue from a female virgin (CBA x DBA/2)F1 mouse which had been unsuccessfully grafted with leukemic tissue from plasma-cell leukemia line 66 at 2 mo. of age, induced generalized leukemia in other mice of the same strain. The karyotype of 10 cells examined in the first passage showed 47 normal chromosomes with no markers. The serum protein of all leukemic mice showed a γ -paraprotein of very slow mobility (seen in the fast γ -region in the original line). Characteristic virus-like particles with "tails" were seen in electron-micrographs of the spleen and plasma which were similar to those described for 2 other leukemias. Pretreatment with i.p. inj. of the virus 32 and 12 days before s.c. inoc. of leukemic cells resulted in longer survival times (30-38 days) than in 4 controls (21 and 22 days). Injection of cell-free medium from tissue culture of line 66 leukemic spleen after 8 mo. gave rise to leukemia in 1/6 mice (spontaneous leukemia in this strain occurs only after 18 mo.). This leukemia is transplantable; the karyotype of 8 cells showed 41, 2 cells 42 chromosomes with no markers present. The serum protein pattern showed no abnormal fractions. Again characteristic virus-like particles were seen.

- 64-1961 ANIMAL AND PLANT VIRUSES WITH DOUBLE-HELICAL RNA. (E.) Gomatos, P. J. (Rockefeller Inst., New York) and I. Tamm. Proc. Nat. Acad. Sci. USA 50(5):878-885, 1963.

The genetic material of plant wound tumor virus (WTV) is a large double-helical RNA, as is that of reovirus. In WTV RNA, the mole% of guanine (G) is 19, adenine 31, cytosine (C) 19, and uracil 31; comparable values for reovirus are 22, 28, 22 and 28, resp. The melting temperature of 90°C for WTV, about 3° lower than that of reovirus RNA in the same medium, probably reflects the lower G + C content in WTV (38%, compared to 44% for reovirus). No serological relationship was found between WTV and any of the 3 prototype strains of reovirus. Reoviruses possess some of the necessary attributes of viruses with tumorigenic capacity.

- 64-1962 ONCOGENIC-INFECTIOUS NUCLEOPROTEIDES AND CARCINOMA OF THE UTERINE CERVIX. (Ger.) Eschbach, W. (Robert-Rössle Clin., German Acad. Sci. Berlin, Berlin-Buch). Acta Biol. Med. German 11(4):560-575, 1963.

Methods are described for the preparation of cell-free nucleoproteide extracts derived from in situ carcinomas of the cervix. Incubation of

these extracts with human embryonic renal tissue cells resulted in cancerization of the host cells. The effect was demonstrable through 3-8 subsequent passages.

- 64-1963 STUDIES ON THE MECHANISM RESPONSIBLE FOR THE SPONTANEOUS REGRESSION OF THE SHOPE RABBIT PAPILLOMA. (E.) Kreider, J. W. (Dept. Path., U. Pennsylvania Sch. Med., Philadelphia). Cancer Res. 23(9):1593-1599, 1963.

A detailed report of the work abstracted as CRA 1(5):#918, 1963.

- 64-1964 FOCUS FORMATION BY JAPANESE QUAIL CELLS INFECTED WITH ROUS SARCOMA VIRUS. (E.) Freeman, G. (Dept. Med. Sci., Stanford Res. Inst., Menlo Park, Cal.). J. Nat. Cancer Inst. 31(4): 761-766, 1963.

Embryonic Japanese quail and chick fibroblasts in secondary cultures were equally efficient in forming foci when infected with Rous sarcoma virus. However, quail monolayers stained with neutral red were more homogeneous and paler than chick monolayers and afforded greater contrast to the deeply stained sarcoma cells. This facilitated identification of foci at low magnification (20x) and reduced scanning time when large numbers of cultures were handled. These infected quail cells appeared to release Rous sarcoma virus.

- 64-1965 PRODUCTION AND RELEASE OF VIRUS-LIKE PARTICLES BY CULTURES OF AGENT-FREE ASCITES CELLS. (E.) Miroff, G. (Rockefeller Inst., New York) and D. G. Feldman. J. Nat. Cancer Inst. 31(4):807-825, 1963.

Cells of a culture of a mouse mammary gland ascite: tumor freed of mammary tumor agent (demonstrated with bioassay by passage in agent-free mice), when propagated i.p. in infected and agent-free hosts, failed to produce type A or B particles when examined with the electron microscope. When propagated for periods up to 31 days, type A particles were found in the cells irrespective of whether the host possessed the agent. Production of virus like particles by monolayer cultures of these cells, when brought in contact with milk preparations containing or devoid of mammary tumor agent, or with buffer alone, was compared with the ability of respective culture fluids to produce mammary tumors when inj. into susceptible agent-free female mice. The presence or absence of A and/or B particles from these cultures could not be correlated with the tumor-producing potential of the material under test. Material inj. for assay contained many B particles. If the B particles are the agent then the number inj. should have resulted in a positive bioassay. Failure to obtain a positive bioassay from the tissue culture fluids in contact with cells propagated in vitro that are producing these particles, morphologically indistinguishable

from those developing *in vivo*, may indicate: 1) their synthesis from components in the media ordinarily foreign to the host imparts sufficient antigenicity to the particles to render them incapable of initiating the oncogenic process, or 2) these particles are a cellular product proliferated as a result of infection by the mammary tumor agent.

4-1966 MIXED INFECTION WITH SIMIAN VIRUS 40 AND ADENOVIRUS 12. (E.) O'Connor, G. T. (NCI, Bethesda), A. S. Rabson, I. K. Berezsky and F. J. Paul. *J. Nat. Cancer Inst.* 31(4): 903-917, 1963.

After 72 hr. of incub. of cultures of African green monkey kidney cells with both SV40 and human adenovirus (AD) 12, approx. 50% of the cells contained many virus particles typical of AD, with no evidence of SV40 particles. About 50% contained many SV40 particles but no AD. In about 1% of the cells, however, large numbers of particles of both viruses, clearly differing in size and morphology, were intermingled within the same nucleus. When the inoc. with AD was delayed for 18.5-24 hr. after the initial infection with SV40, the number of cells producing both viruses was substantially increased. But if the subsequent inoc. of AD was withheld for 1 hr., a predominance of cells infected with SV40 alone was seen and only a relatively small percentage of cells containing both viruses was found. These observations indicate that mixed infection with SV40 and AD 12 can occur and that variable degrees of partial exclusion may be produced.

4-1967 VIRAL SUSCEPTIBILITY AND EMBRYONIC DIFFERENTIATION. III. CORRELATION BETWEEN AN INDUCTIVE TISSUE INTERACTION AND THE ONSET OF VIRAL RESISTANCE. (E.) Vainio, T. (Dept. Physiol. Zool., U. Helsinki), L. Saxén and S. Toivonen. *J. Nat. Cancer Inst.* 31(6): 1533-1547, 1963.

Viral resistance in connection with tubulogenesis was studied. Tubules were induced in metanephrogenic mesenchyme with an artificial inducer (spinal cord), and SE polyoma virus was applied to this system during differentiation *in vitro*. The distribution of this virus was demonstrated by the immunofluorescence technic. The mesenchyme that was not induced to form tubules synthesized polyoma antigen. Of the mesenchymal cells "left out" of the differentiation process, those enclosing the tubules seemed to support the rapid synthesis of viral protein. The epithelial cells in the tubules were not able to synthesize viral protein at any stage of infection, thus appearing resistant to polyoma virus. It was established from these experiments that the mesenchymal cells which undergo tubulogenesis fail to support the replication of polyoma virus *in vitro*.

64-1968 FLUORESCENT ANTIBODY STUDIES OF THE VIRAL ANTIGEN IN A MURINE LEUKEMIA (RAUSCHER). (E.) Fink, M. A. (NCI, Bethesda) and R. A. Malmgren. *J. Nat. Cancer Inst.* 31(5):1111-1121, 1963.

Malignant lymphoid tissues of BALB/c mice and Osborne-Mendel rats infected with Rauscher virus (RNC1-2) contained viral antigen reactive with fluorescent antibody. The specific fluorescence occurred intranuclearly and less constantly in the cytoplasm. Absorption of the fluorescein labeled rabbit-anti-RNC1-2 globulin with infected mouse spleen (but not normal spleen), effectively prevented the specific fluorescence. In addition to the fluorescence in the malignant lymphoid cells, mature megakaryocytes of infected rat bone marrow contained specific nuclear, but no cytoplasmic, fluorescence. Cells from normal mice and rats, from transplantable lymphatic leukemias and reticulum cell sarcomas not known to be associated with a virus, and from DBA/2 mice infected with Friend virus did not react with the RNC1-2 antiserum.

64-1969 CHROMOSOME STUDIES OF VIRUS-INDUCED RABBIT PAPILLOMAS AND DERIVED PRIMARY CARCINOMAS. (E.) McMichael, H. (Dept. Path., U. Pennsylvania Sch. Med., Philadelphia), J. E. Wagner, P. C. Nowell and D. A. Hungerford. *J. Nat. Cancer Inst.* 31(5):1197-1215, 1963.

The chromosomes of 25 primary epidermal rabbit tumors, induced by the Shope virus, were studied in various stages of development from early benign papillomas to invasive carcinomas. Abnormalities of chromosome structure, including the presence of cytogenetically altered stemlines, were observed at all stages. The incidence and extent of such change increased with time and with the conversion to malignancy, usually being well advanced at the time of, or prior to, invasion. No consistent abnormalities were seen at any stage. Hence, the changes observed were probably not causally related to the initiation of the neoplasm, and their significance with respect to the subsequent development of malignancy remains obscure.

64-1970 FURTHER STUDIES ON KARYOTYPES OF A VARIETY OF PRIMARY AND TRANSPLANTED MOUSE POLYOMA TUMORS. (E.) Hellström, K. E. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm, Sweden), I. Hellström and H. O. Sjögren. *J. Nat. Cancer Inst.* 31(5):1239-1253, 1963.

Karyologic studies were made on 5 primary and 18 transplanted tumors induced by polyoma virus in mice. Stemlines of 16 were changed chromosomally and most often were different for each neoplasm, while 7 tumors, 1 of which was primary, contained cells with the normal diploid number of 40 as their stemline and did not show any detectable structural modifications. Four diploid tumors,

followed through several passages, became aneuploid. On the other hand, aneuploid stemlines generally remained constant during prolonged propagation *in vivo*. All tumors varied considerably around the stemline chromosome numbers. The results show that such chromosomal changes cytologically detectable in telocentric mouse chromosomes are not prerequisite for the neoplastic transformation by the polyoma virus, but apparently often give the cells selective advantage. No systematic chromosome changes distinguished polyoma tumors from tumors where no viral etiology is known.

64-1971 ELECTROPHORETIC SEPARATION OF THE MOUSE MAMMARY TUMOR VIRUS. (E.)

Moore, D. H. (Rockefeller Inst., New York) and M. J. Lyons. *J. Nat. Cancer Inst.* 31(5):1255-1273, 1963.

A method is described for the isolation of the B particles in milk, which show greater electrophoretic mobility at neutral pH than any of the other main components. A special electrophoresis tube with pH and density gradients is employed.

64-1972 ANTIGENIC CHARACTERISTICS OF THREE VARIANTS OF ROUS SARCOMA VIRUS. (E.)

Simons, P. J. (Imperial Cancer Res. Fund, Mill Hill, London, N.W. 7) and R. M. Dougherty. *J. Nat. Cancer Inst.* 31(5):1275-1283, 1963.

Three antigenic variants of Rous sarcoma virus are described by use of a neutralization test. Strain RSV(H) showed little or no cross-neutralization; there was partial cross-neutralization between the remaining two variants, RSV(B) and RSV(29). Antiserum prepared in turkeys was less specific than chicken antiserum, i.e., turkey antisera cross-neutralized more frequently and showed higher levels of cross-reaction. Chicken serum having "naturally occurring" antibodies neutralized RSV(B) but not RSV(H). Rous antibody-free chicken serum failed to neutralize either of the major antigenic types.

64-1973 BIOLOGICAL PROPERTIES OF THREE VARIANTS OF ROUS SARCOMA VIRUS. (E.)

Dougherty, R. M. (Dept. Microbiol., State U. New York, Upstate Med. Ctr., Syracuse), P. J. Simons and F. C. Chesterman. *J. Nat. Cancer Inst.* 31(5):1285-1307, 1963.

The responses to 3 antigenic variants of Rous sarcoma virus (designated RSV(B), RSV(H), and RSV(29)) have been compared in 4 host systems. On the chorioallantoic membrane, RSV(B) induced relatively opaque pocks about 1.5x the diameter of those initiated by the other 2 strains. While the pocks were qualitatively similar with all 3 strains, a greater proportion of those induced by RSV(B) showed involvement of the mesoderm and entoderm. Cornification of the ectoderm was

most frequent with RSV(29). Tissue cultures of chick embryo fibroblasts infected with RSV(B) or RSV(29) developed typical round cell foci, and plating efficiency in the tissue culture assay was high. With RSV(H), tissue cultures developed diffuse foci of elongated cells, which were impossible to count accurately, and plating efficiency was 10% or less compared with the chorioallantoic membrane assay. In 7- to 8-week-old turkeys, RSV(B) and RSV(29) induced tumors that increased in size throughout a 10 wk. period. By 10 wk., more than 50% of the birds infected with RSV(B) had gross tumors at sites other than the point of inoc., but none of the turkeys infected with RSV(29) developed secondary tumors in this period. Turkey tumors induced by RSV(H) grew for about 2 wk., then rapidly regressed, and gross metastases were not seen. The responses of 1-week-old Brown Leghorn chickens to all 3 strains were similar with respect to latency after use of both high and low doses of virus. All tumor growth rates were the same, although RSV(B) tumors reached somewhat larger size. Highest virus content was in RSV(B) tumors. Histologically, tumors induced by the 3 viruses were identical.

64-1974 HUMAN SUSCEPTIBILITY TO A SIMIAN TUMOR VIRUS. (E.)

Grace, J. T., Jr. (Roswell Park Mem. Inst., Buffalo, N. Y.) and E. A. Mirand. *Ann. N.Y. Acad. Sci.* 108(Art. 3):1123-1128, 1963.

The hand of a healthy young male laboratory worker was accidentally punctured by a needle contaminated with a simian tumor virus (which initially was noted in a monkey colony in Yaba, Nigeria). Complement-fixing antibody appeared in his serum within 1 wk., rose progressively for 3 wk. and then remained at that level for 4 mo. at which time he developed a nodule at the site of needle puncture. The nodule grew rapidly for 7 days at which time it was removed; it had reached a diameter of 2 cm. Histologically it was similar to the typical monkey lesion and virus was readily recovered from it. The serum antibody level gradually diminished over the ensuing 3.5 mo. to a level where it was no longer detectable. The pt. has been observed for 2 yr. after excision of the lesion and has had no further difficulty. (For an earlier study of this virus see CRA 1(2):#268, 1963.)

64-1975 TUMOR VIRUS STUDY SYSTEMS. (E.)

Huebner, R. J. (NIH, Bethesda). *Ann. N.Y. Acad. Sci.* 108(Art. 3):1129-1148, 1963.

After a brief discussion of tumor viruses (papov group, adenoviruses, pox viruses, leukemia group and their natural and other hosts, a comparison is made of the occurrence of a number of viruses in man, monkey, mice, cattle and chickens. Especially impressive is the fact that the common mouse (*Mus musculus*), perhaps the most commensal of man's animal associates, also reveals a patte

of viral infections which mirror those of man. In a study of this mouse in the wild state, so far, none of these viruses have been found. In a discussion of cancer viruses in nature, transmission of avian leukosis (an RNA virus) is briefly reviewed. Also reviewed are studies in the detection of mouse polyoma virus (a DNA virus) in laboratory colonies. These studies have now been extended to urban ecologies in New York City. Fairly large mouse populations in the Boroughs of Queens and the Bronx previously shown to harbor rickettsial pox and lymphocytic choriomeningitis viruses were found to be negative for polyoma. However, studies of larger and more dense mouse populations in Harlem revealed numerous polyoma infected areas. In all, about 20% of nearly 800 mice collected from a number of buildings were positive. Polyoma virus was isolated from the tissues and urine of serologically positive mice, from nesting materials and from floor and shelf sweepings containing visible mouse droppings. Similar studies were made of rural ecologies where again polyoma positive mice were found in some farms and grain mills where there were large mouse populations. In both the urban and rural studies, other viruses were found in some mice (Reo 3, Theiler's, CM, K, mouse adenovirus, mouse hepatitis and pneumonia virus of mice). In a limited survey of a few adult humans and cattle exposed to infected and contaminated grain, serological studies have been negative. Some of the implications of this close and long association of man with grain contaminated by the excreta of the house mouse are discussed.

1976 A PRELIMINARY STUDY ON TISSUE CULTURES OF BOVINE LYMPHOSARCOMA. (E.)
 tzolios, B. C. (Vet. Sci. Dept., U. Maryland, College Park) and S. C. Chang. Ann. N.Y. Acad. Sci. 108(Art. 3):1214-1230, 1963.

Issue from a tumor mass of a pure bred Holstein cow affected with generalized lymphosarcoma was cultured in Eagle's minimum medium supplemented 10% of inactivated normal calf serum. The cells of this culture and of 5 subcultures preserved their resemblance to the primitive reticular cells of the tumor and thus were distinguished from cells cultured from normal lymph node tissue. Lymphosarcoma tissue extracts of 2 cows in dilutions up to 10^{-4} caused changes in normal lymph node monolayers suggestive of a cytopathogenic agent; this effect persisted in the second successive passage on this monolayer. Transmission studies to one-day-old calves and newborn Swiss mice are reported utilizing cell emulsion, tissue cultures, and extract of tissue taken from an infected cow. Among mice inj. intracerebrally with extract, a high incidence of lymphocytic leukemia with relatively short latency was observed (in contrast to groups inj. i.p. and in thymic area). This result is suggestive of the existence of an agent. The morphologic changes seen in cell cultures, the development

of cytopathogenic effect in monolayer cultures and the presence of fluorescent bodies which were noted in cultured cells could be interpreted as suggestive of the involvement of a specific agent in the etiology of bovine lymphosarcoma.

64-1977 REGARDING THE DEVELOPMENT OF THE CYTOPATHOGENIC EFFECT OF MOUSE EMBRYONAL CULTURES BY THREE DIFFERENT STRAINS OF POLYOMA VIRUS. (Ger.) Georgii, A. (Inst. Path., U. Munich, Germany) and H. Wrba. Zschr. Krebsforsch. 65(6):582-589, 1963.

When polyoma virus strain BBT2 of Graffi, that of Stewart and that of Rowe were grown in cultures of fibroblasts, while the infectious titer for all was equally high, there were distinct differences in the cytopathogenic effect (CPE). The Graffi polyoma virus resulted in mostly the so-called defective form of CPE which occurred relatively quickly and led to the rapid destruction of the entire cell culture. The Stewart and Rowe polyoma virus strains induced a more slowly developing so-called rarefying form of CPE which was difficult to differentiate from nonspecific changes.

64-1978 PREVENTION OF LYMPHATIC LEUKEMIA IN THE CHICKEN BY THE SURGICAL REMOVAL OF THE BURSA OF FABRICIUS. (E., Abstract) Petersen, R. D. A., B. R. Burmester, T. N. Fredrickson and R. A. Good. J. Lab. Clin. Med. 62(6):1000, 1963.

Chickens from the isolated line 15 at the Regional Poultry Laboratory were infected with a filtrate of RPL 12 L 31. It was found that bursectomy performed at hatching or at 1 mo. of age would almost completely eliminate the occurrence of visceral lymphomatosis (VL); thymectomy alone had no effect. Thymectomy + bursectomy had no significantly greater effect on VL than did bursectomy alone. From 60-70% of sham-operated chickens developed VL. Approx. 50% of all the lots developed erythroblastosis regardless of their surgical history. Only the lymphocytic type of leukemia was prevented by bursectomy.

64-1979 ON THE NEORICKETTSIAL (MIYAGAWANELLOUS) ETIOLOGY OF LYMPHOGRANULOMATOSIS (HODGKIN'S DISEASE). (Ger.) Kujumgiev, I. (Inst. Microbiol., Bulgarian Acad. Sci., Sofia). Zbl. Bakt. (Orig.) 190(1):27-33, 1963.

A German version of the paper originally published in Bulgarian and abstracted as CRA 1(9-10):#1742, 1964.

64-1980 EARLY INFLUENCE OF POLYOMA VIRUS ON TRANSPLANTED TOOTH GERMS. (E.)
 Nagai, I. (Dept. Oral Maxillofacial Surg., Osaka U. Dent. Sch., Japan), W. Yoshioka, M. Kumegawa, J. Arita and J. Ikeda. J. Dent. Res. 42(5):1131-1139, 1963.

Fetal tooth germs of dd0 mice at 15 days of gestation were exposed to polyoma virus (by incub. for 2 hr. with tissue culture media containing the virus) and then transplanted into the axillas of 2-month-old female dd0 mice. Control tooth germs were exposed to uninfected tissue culture medium. The survival of the transplants was not affected by virus exposure, and no tumors of the axilla or other organs were observed in the transplant hosts. After exposure to low virus titers differences were observed in the histologic appearance of virus-treated tooth germs, including inhibition of enamel matrix, stratum intermedium and stellate reticulum formation, and loss of cellular activity, polarity, and columnar appearance of the inner enamel epithelium, with squamous metaplasia in the occlusal plane. Dentin formation in the occlusal plane was not inhibited, but the odontoblasts showed slight degeneration. Maximal inhibition of development was observed at 20 to 25 days. The changes were more striking and appeared at an earlier time when a higher titer of virus was used in the pre-transplant procedure. Here at 20-25 days osteoid-like tissue resembling bone was observed in place of dentin.

64-1981 INCORPORATION OF DNA INTO A MOUSE TUMOR IN VIVO AND IN VITRO. (E.)

Rabotti, G. F. (Dept. Path., Jefferson Med. Coll., Philadelphia, Pa.). Exp. Cell Res. 31(3):562-565, 1963.

The specific activity of the bases of C^{14} -formate labeled DNA from BDFIT ascites tumor was different from that of DNA of the same tumor cells grown in vitro. This radiochemical marking has been utilized to study the penetration of DNA molecules into living cells. Under certain conditions, it would appear that this is likely to happen. This radiochemical marking can thus be used as a tool for the study of mammalian cell transformation.

64-1982 INDUCTION OF SUBCUTANEOUS FIBROMAS IN GOLDEN HAMSTERS BY INOCULATION OF CELL-FREE EXTRACTS OF BOVINE PAPILLOMAS. (Fr.)

Friedman, J.-C. (Leukemia Res. Inst., Saint-Louis Hosp., Paris), J.-P. Lévy, J. Lasneret, M. Thomas, M. Boiron and J. Bernard. C. R. Acad. Sci. 257(16):2328-2331, 1963.

Although no tumors of any kind appeared in 14 golden hamsters inoc. with extracts of healthy skin, or in 42 untreated controls, 15/16 2-day-old hamsters inoc. with cell-free extracts of calf papilloma (1-21 days after preparation of the extracts) by intrascapular scarification and instillation of 1 drop of extract into the 3-5 mm wound, developed single or multiple fibroma at the site of inoc. Identical results were obtained in a parallel series, and in C3HeB mice, by s.c. inoc.; one hamster inoc. intrathoracically developed true papillomas of the face and all 4 limbs, 7 mo. after inoc. The authors point out

that these studies suggest, but do not necessarily confirm, a viral origin of bovine papilloma.

64-1983 IN VITRO TRANSFORMATION OF EMBRYONAL CALF SKIN CELLS UNDER THE ACTION OF

CELL-FREE EXTRACTS OF BOVINE PAPILLOMAS. (Fr.) Thomas, M. (Leukemia Res. Inst., Saint-Louis Hosp., Paris), J.-P. Lévy, J. Tanzer, M. Boiron and J. Bernard. C. R. Acad. Sci. (Paris) 257(15):2155-2158, 1963.

A marked acidification of the culture medium was seen from the very first days following inoc. of embryonal calf skin monolayer cultures with cell-free extracts derived from 2 different bovine papillomas which had been shown to be rich in virus particles. About 45 days following inoc. with the cell-free papilloma extract, the monolayer cultures showed many very elongated cells, which rapidly multiplied in all planes and appeared visible to the naked eye as small white plaques. Microscopic examination showed a disorderly arrangement of cells. This multiplication progressed rapidly; 15 days later, the plaques covered the whole culture. Trypsinization of the monolayers (and subsequent growth of new cultures) 60 days after extract inoc. resulted in cells which also grew very rapidly and which produced intense acidification of the new culture media. No further modification of the transformed cells occurred after 14 passages. Cells derived from untreated controls were lost after passage 3 and survival of 4 mo. Intranuclear inclusions were not found in the transformed cells, nor were there changes in the modal number of 60 chromosomes. Transplantation of 10^6 transformed cells into the cheek pouch of the hamster had not given rise to tumors after 7 wk. of observation.

64-1984 CATTLE LEUKOSIS IN GERA PROVINCE.

(Ger.) Meyer, H. (Res. Inst. Bact. Dis. Animals, German Acad. Agric. Sci., Berlin). Arch. Exp. Veterinaermed. 17(4):799-817, 1963.

Statistical data for the yr. 1958 to 1961 show a high conc. of cattle leukosis in the northeast districts of the Gera province. The disease appears to be virus-induced and transmitted to the calves through the placenta or through the milk, and should be differentiated from the calf leukosis which is highly sporadic and is not limited geographically to defined regions.

64-1985 VIRUS-LIKE PARTICLES IN BLOOD OF TWO ACUTE LEUKEMIA PATIENTS. (E.) Almeida

J. D. (Ontario Cancer Inst., Toronto, Canada), R. C. Hasselback and A. W. Ham. Science 142: 1487-1489, 1963.

A modified negative staining technic revealed, by electron microscopy, particles having a surrounding membranous sac and an internal filamentous

component (7.5 μ in diameter) in the peripheral blood of 2 pts. with acute leukemia. Similarly prepared samples of blood from 4 other pts. with acute leukemia and 6 normal individuals did not show this type of particle.

64-1986 CONTRIBUTION ON TUMOR FORMATION IN WILD LIVING BIRDS. (Ger.) Groth, W. Inst. Anat. Physiol. Domestic Anim., Rhein. Friedrich-Wilhelms-U. Bonn, Germany). Berlin. Tierärztl. Wschr. 76(10):192-194, 1963.

Histological examination of the nodules on the legs of a pair of crested larks (found in Spain) revealed, besides hyperplasia of epithelial tissue due to chronic inflammation, some areas of malignant infiltrative growth of epithelial cells. Atrophic degeneration of epithelial cells, eosinophilic cytoplasmic inclusion bodies and lymphocytic, plasmacytic and histiocytic infiltration of the corium, subcutis and tumor stroma suggest that owl pox virus might have been the causative agent.

64-1987 TRANSMISSION OF VIRUS FROM FIELD CASES OF AVIAN LYMPHOMATOSIS. I. ISOLATION OF VIRUS IN LINE 151 CHICKENS. (E.) Burmester, B. R. (Regional Poultry Res. Lab., East Lansing, Mich.) and T. N. Fredrickson. J. Nat. Cancer Inst. 32(1):37-63, 1964.

Transmissibility of various tumors collected from farm and experimental flocks of chickens was tested in day-old line 151 chicks by intraperitoneal inoc. of tumor extracts, oral washings, and plasma. The animals were observed for 245 days. Cell-free inoculums from 10 of the 19 flocks induced a total neoplastic mortality of more than 50%. An extract of a nephroblastoma also caused a high incidence of neoplasms. Material from neural lymphomatosis and ocular lymphomatosis induced moderate neoplastic mortality. Most of the mortality was from visceral lymphomatosis and to a lesser extent from erythroblastosis. Most sources also caused osteopetrosis and a few fibrosarcomas and endotheliomas. Sporadic cases of neural lymphomatosis but none of nephroblastoma or myeloblastosis were observed. There appeared to be no correlation between oncogenic activity of the inoculums and the breed, the age of the donor birds or size and type of flock. Fairly uniform quantitative and qualitative responses were induced by the more potent isolates obtained from cases of visceral lymphomatosis from flocks with a high incidence of this disease. The responses were similar to those induced by a low dose of the RPL12 strain avian tumor virus.

64-1988 TUMORS PRODUCED BY ADENOVIRUS 12 IN MASTOMYS AND MICE. (E.) Rabson, S. (NCI, Bethesda), R. L. Kirschstein and J. Paul. J. Nat. Cancer Inst. 32(1):77-87, 1964.

Newborn Mastomys (*Rattus natalensis*) and newborn C3H/BI mice were inoc. with human adenovirus 12, some s.c., some intracerebrally, and some by both routes. Tumors were observed in 2/32 Mastomys after 5-6 mo. and in 7/29 mice after 2.5-6 mo. Histologically, the tumors were similar to those described by Trentin and his associates and by Huebner and his associates in Syrian hamsters inoc. with adenovirus 12, and were classified as "undifferentiated malignant tumors". Transplantation of one of the mouse tumors was attempted, and it was serially transplantable in C3H/BI mice. Attempts to isolate virus from the tumors were unsuccessful.

64-1989 VIRUS OF AVIAN MYELOBLASTOSIS (BAI STRAIN A). XXV. ULTRACYTOCHEMICAL STUDY OF VIRUS AND MYELOBLAST PHOSPHATASE ACTIVITY. (E.) De Thé, G. (Duke U. Med. Ctr., Durham, N. C.), C. Becker and J. W. Beard. J. Nat. Cancer Inst. 32(1):201-235, 1964.

Ultracytochemical studies showed nucleosidetriphosphatase reaction at cell membranes of myeloblasts of myeloblastic leukemia induced by BAI strain A virus and no reaction for adenosinediphosphatase. Cytoplasmic gray bodies were positive for triphosphatase, diphosphatase, and acid phosphatase. Myeloblasts liberated BAI strain A virus by cytoplasmic membrane budding, and more than 90% of the particles were nucleosidetriphosphatase-positive and diphosphatase-negative. The present and other recent findings suggested that myeloblast gray bodies represent lysosome-like digestive organelles rather than loci of virus synthesis as formerly speculated. Identical phosphatase activity of virus and cell membrane indicated origin of virus enzyme by cell-membrane incorporation in the budding process. A small proportion of strains R and ES4 avian tumor virus particles exhibited lead phosphate precipitate at the surface, and this may have been related to enzyme-positive extraneous material in the preparations. The possible nature and origin of gray bodies are discussed.

64-1990 STRAIN DD, A NEW HIGH MAMMARY TUMOR STRAIN, AND COMPARISON OF DD WITH STRAIN C3H. (E.) Heston, W. E. (NCI, Bethesda), G. Vlahakis and Y. Tsubura. J. Nat. Cancer Inst. 32(1):237-251, 1964.

Strain DD is a new high mammary tumor strain unrelated to other high mammary tumor strains in origin. It has the mammary tumor virus. The incidence of mammary tumors in DD is high, although not quite so high as in C3H, but, like in C3H, the incidence is high in virgin females as well as in breeders. Data presented show that strain C3HFB (C3H without the mammary tumor virus) continues to have a median incidence of mammary tumors in breeding females of a relatively old age, which is believed to be the result of high genetic susceptibility and hormonal stimulation

from breeding in the absence of the mammary tumor virus. Reciprocal foster-nursing between DD and C3H and the use of fostered virgin C3HfB females for assay demonstrated that the mammary tumor virus of DD was weaker either qualitatively or quantitatively than that of C3H. There was no consistent evidence that the strains differed in their genetic susceptibility to the virus. The most interesting characteristic of females of DD is the progression and regression of some of their mammary tumors involving early plaque formation in relation to pregnancy, as described by others for strain RIII and RIII hybrids.

64-1991 VIRAL STUDIES OF SV40 TUMORIGENESIS IN HAMSTERS. (E.) Black, P. H.

(Natl. Inst. Allergy Infect. Dis., Bethesda, Md.) and W. P. Rowe. J. Nat. Cancer Inst. 32(1):253-265, 1964.

After s.c. inoc. into newborn hamsters, SV40 virus rapidly declined in titer and could not be detected between the 10th postinoculation day and the time of tumor development, 4 mo. later. Frequency of virus recovery from tumor extracts appeared to be related to tumor size; 31% (4/13) of small tumors, 62% (16/26) of medium tumors, and 25% (5/20) of large tumors yielded virus, with titers highest in the medium-sized tumors. Neutralizing antibody developed proportionally to tumor size, even in several animals which had serial tumor biopsies consistently negative for virus; this antibody was probably largely responsible for lack of virus isolation from large tumors. The failure to recover virus during the latent period may be a manifestation of the highly integrated cell-virus relationship found in SV40 tumor cells.

64-1992 THE PROBLEM OF THE PHAGE-LIKE STRUCTURE OF THE AVIAN LEUKOSIS VIRUS. (E.)

Bartl, P. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague), J. Říman and F. Šorm. Experientia 19(12):635-637, 1963.

The proportion of tailed phage-like forms of BAI strain A virus passed in white Leghorn chickens

was max. (80-85%) when 24-33% myeloblasts could be found in the blood of the animal. This period represented the time of sharpest increase in the level of leukemic cells in the blood. When there were more than 35% leukocytes in the blood, there was an irregularity in the relation between the total mass of the myeloblasts and their numbers. This indicated to the authors that there was a cell population with a continuous growth in cell mass but with decreased mitotic activity. There appeared to be no relationship between the number of tailed or spherical particles observed and the method used to dry the preparation (colloid membrane or agar technic). The effect of different types of isolation solutions were in agreement with reports in the literature.

64-1993 INHIBITION OF MOUSE TUMOR TRANSPLANTS BY POLYOMA VIRUS INOCULATION. (E.)

Mirand, E. A. (Roswell Park Mem. Inst., Buffalo, N. Y.), J. T. Grace, Jr. and J. G. Hoffman. Virology 21(1):56-60, 1963.

Polyoma virus inoc. of adult male DBA/1 mice conferred resistance to subsequent transplantation of 3 isologous tumors: a chemical carcinogen-induced (9,10-dimethyl-1,2-benzanthracene; DMBA) sarcoma, a spontaneous mammary adenocarcinoma, and a polyoma virus-free parotid tumor originating in a mouse inoc. at birth with polyoma virus. A tumor cell inocula causing 100% tumor takes and killing times decreasing with increasing inoculum dose, infection i.p. with polyoma virus 40 days previously caused a tumor cell inoculum dose-related decrease in tumor takes and an increase in survival times. For the DMBA-induced sarcoma, spontaneous mammary, and parotid tumors, resp. The inhibitory effect was observed between $78-45 \times 10^3$, $83-38 \times 10^3$ and $76-24 \times 10^3$ tumor cell inocula. However, when the tumor inoculum was increased significantly by the use of tumor fragments, resistance in virus preinoculated mice was masked, and no significant difference was observed between the experimental and control groups. The basis for the observed cross resistance has not been established, although several possible mechanisms are discussed.

See also abstract nos.: 1840, 1843, 1845, 1848, 1850, 1858, 1862, 1883

EPIDEMIOLOGY AND BIOMETRY

64-1994 MALIGNANT NEOPLASMS IN CHILDHOOD AND YOUTH. INCIDENCE IN THE NORWEGIAN POPULATION UNDER 20 YEARS OF AGE BETWEEN 1953-1958. (Nor.) Bjelke, E. *Nord. Med.* 70(27): 770-774, 1963.

As of 1951, Norwegian law has required the registration of all new cases of cancer. A review of the resulting statistics for the yr. 1953-58 showed a progressive gradual decline of the incidence of cancers in males from age 1 to age 11, except for a slight (and probably statistically nonsignificant) rise at age 3. From age 11 to age 19, the rate increased progressively, rising sharply from 16 on and reaching the first year level (approx. 19/100,000) again by age 20. In females, a similar, initial decline terminated about age 7; was followed by a gradual increase to age 13, and by a second decline between ages 15 and 17. At age 20, the rate of incidence was approx. 60% of the first yr. level (i.e. 10 vs. 8/100,000). Between 9 and 13, the rate of incidence was somewhat (but not markedly) higher among girls; between 13 and 15, no sex difference was demonstrable; and at all other times, the rate was higher among boys. Leukemia accounted for 30.5% of all cancers developed in the first 10 yr. of life; intracranial tumors for 22.5%; non-leukemic cancers of the lymphatic system for 1.6%. However, a breakdown by 4-yr. periods 0-4, 5-9, 10-14, and 15-19 showed these overall data were misleading. In these age groups, intracranial tumors accounted for 17.0, 33.5, 26.3, and 16.9% of all cancers, resp.; the leukemias for 42.2, 29.3, 25.2, and 14.2%, resp.; non-leukemic cancers of the lymphatic system for 5.9, 11.5, 14.5, and 20.3%, resp. Age-specific incidence rates are reported for a total of 27 primary sites. The author concludes that such diagnostic statistics for specific age-groups and areas (as contrasted to reported death-rates) are essential for further progress in the fields of carcinogenesis and cancer epidemiology.

64-1995 LUNG CANCER MORTALITY IN THE NETHERLANDS. (Dut.) Meinsma, L. *Nederl. T. Geneesk.* 107(32):1432-1436, 1963.

In the Netherlands, a study of regional mortality due to lung cancer in men, 1956-60, showed that the rates (per 100,000 of male population) were significantly higher in the industrialized western provinces of North Holland (60), South Holland (53), and Utrecht (46) than the national av. (42), while significantly lower rates were found in the relatively non-industrialized provinces of Groningen (30), Friesland (29), Drente (20), and IJsselmeer-Polders (6). From the epidemiological point of view, "foci" of incidence were found in the large industrial areas of Haarlem (73), Amsterdam (69), 's-Gravenhage (63), Rotterdam (62), and Utrecht (50); in each case there was a reading toward the northeast. In all areas,

the mortality rate appeared to be directly proportional to the degree of air pollution, including pollution due to motor vehicles on the canals and highways. A study of the possible relation of lung cancer deaths to cigarette consumption (g/person/year, in terms of the total population in 1960) showed a national av. (excluding IJsselmeer-Polders, for which data were not available) of 1,047 (in men who were 45 or older in 1958). In the high-incidence cities of Amsterdam, Rotterdam and 's-Gravenhage, consumption was 1,586; in the high-incidence provinces of North Holland, South Holland, and Utrecht (exclusive of the above cities) it was 999; in low-incidence provinces of Groningen, Friesland, and Drente, it was 873. The author concludes that further research into the role of air pollution in carcinogenesis is clearly indicated.

64-1996 SMOKING AND HEALTH. (E.) The Surg. Gen. Advisory Comm. on Smoking and Health. U.S. Dept. Health, Educ., Welfare, Public Health Serv. Publ. No. 1103, 387 pp., \$1.25, 1964.

The first 5 chapters in part II ("Evidence of the relationship of smoking to health") are of especial value to those interested in carcinogenesis. After a short presentation on the consumption of tobacco products in the U.S. (3 references), many aspects of the chemistry of tobacco and tobacco smoke are explored with detailed treatment of carcinogenic hydrocarbons and heterocyclics in tobacco smoke, cocarcinogens, mechanism of formation of carcinogens and effect on cilia (51 references). A separate chapter deals with the pharmacology and toxicology of nicotine (24 references). While the chapter on mortality makes use of some well-known published studies, in some cases additional data has been collected, which gives these studies added value. As in other sections, good use is made of tables: 30 are employed in this chapter (17 references). The most extensive chapter, on Cancer (137 pages) deals with various epidemiological aspects of cancer morbidity and mortality, carcinogenesis (problems, effects of tobacco and tobacco smoke in animals, effects of polycyclic aromatic hydrocarbons in man and effects of certain industrial products), and concludes with an extensive treatment of cancer by site (392 references). Also employed in this chapter are 10 figures, 1 illustration and 17 tables. Other chapters deal with other non-neoplastic respiratory diseases, cardiovascular diseases, characterization of the tobacco habit and beneficial effects of tobacco, psycho-social aspects of smoking and finally a consideration of the morphological constitution of smokers. In brief the book is a collection of much valuable material relating to many aspects of the problem of smoking and its impact on our society.

64-1997 EPIDEMIOLOGY OF CANCER OF THE CERVIX IN ROSARIO AND THE ANTI-CANCER CAMPAIGN

OF THE DEPARTMENT OF GYNECOLOGY. (Sp.) Casas, P. F., R. Pecorone, H. Navarini, E. Cerro, J. Medina, M. Franco and E. de Farina. Sem. Med. (B. Air.) 122(37):1450-1451, 1963.

By the examination of the public records of Rosario, Argentina, the authors were able to find that the mortality due to cancer increased 3-fold during the years from 1887 to 1961 (from 47.1 to 155.7/100,000. The incidence of death by cancer in women (1931-1960) was 39.6%, which was lower than that for men. Gynecological cancer accounted for 26.7% of all cancer deaths in women during the period 1951-60 and for 32.4% during the year 1961. During those periods, as many women died of mammary cancer as of gynecological cancer. It was found that endometrial cancer was 4 times less frequent than cervical cancer. This overall incidence was similar to that seen in hospital records (1:5) but very different from that seen in private practice (1.3:1). New case findings are also reported for 3 different methods of survey (multiple biopsies, Papanicolaou, selective biopsies) and these figures are projected into the probable incidence of undetected tumors in the population.

64-1998 EFFECT OF ARSENIC TRIOXIDE ON MORTALITY. (E.) Pinto, S. S. (Am. Smelt. Ref. Co., Tacoma, Wash.) and B. M. Bennett. Arch. Environ. Health (Chicago) 7(5):583-591, 1963.

A study has been made in a Washington State copper smelter of the causes of death among present and pensioned employees dying in the period 1946-1960. A previous study had shown that men not exposed to arsenic excreted an av. of 0.13 mg As/liter of urine; those exposed excreted an av. of 0.82 mg As/liter of urine. There was no evidence that chronic arsenic trioxide exposure of the amount described is a cause of systemic cancer in humans.

64-1999 GASTRIC CANCER: A MIDCENTURY LOOK. (E.) Eisenberg, M. M. (Dept. Surg., U. Florida Coll. Med., Gainesville) and E. R. Woodward. Arch. Surg. (Chicago) 87(5):810-824, 1963.

In a paper devoted in part to the diagnosis and treatment of carcinoma of the stomach, a review (113 references) is presented of epidemiological studies which have attempted (unsuccessfully) to explain the known decrease in deaths in the USA from gastric cancer between 1933 and 1950. Spontaneous gastric carcinoma is extremely uncommon among lower animals (none in 100,000 rats autopsied, 1 adenoma among 381 baboons). Also extensively reviewed is the possible association of 4 benign conditions of the stomach (achlorhydria and chronic gastritis, adenomatous polyps and chronic gastric ulcer) with gastric carcinoma and with one another. Many workers believe that a gastric ulcer is malignant from the beginning or never undergoes malignant change.

64-2000 MALIGNANT MOLES IN CHILDHOOD. (E.) McGovern, V. J. (Royal Alexandra Hosp. Child., Sydney, Australia) and E. Goulston. S. Afr. Cancer Bull. 7(3):87-90, 1963.

Among 189 males and 289 females with the diagnosis of melanoblastoma made at the Royal Prince Alfred Hospital between 1950 and 1961, site of the lesion was, resp.: head and neck, 27.5 and 30.1%; upper limb 15.3 and 12.4%; lower limb 18 and 36.3%; trunk 29.1 and 11.1%; mucosa 2.1 and 2.8%; unknown 8 and 7.3%. Twelve pts. were under the age of 20 yr. From a study 8 cases in children, the authors believe that moles of congenital or nevoid type may become malignant independently of solar exposure. Acquired nevi which become malignant are mainly the result of excessive solar exposure in fair-skinned persons. One example of this type was seen in a child who suffered from xeroderma pigmentosum.

64-2001 SOME INFERENCES ABOUT THE ORIGIN OF TUMOURS DERIVED FROM THEIR AGE DISTRIBUTION. (E.) Smither, D. W. (Roy. Cancer Hosp., London). Clin. Radiol. 14(4):418-423, 1963.

Utilizing many morbidity studies from England and other parts of the world, the thesis is developed that the more common sites for tumor development are those where repeated demands are made for normal growth, either for the repair of damage done or for hypertrophy to meet some functional demand. The battle to maintain structural stability in the face of the environment sets the main pattern of rising tumor age incidence in many long-lived communities. The better control of environment (such as clean air and cessation of smoking) would decrease stresses on tissues and should lead to reduction in tumors. A better understanding of the underlying forces in the production of tumors of the g.i. tract, particularly the stomach, should also be rewarding.

64-2002 MALIGNANT TUMORS IN CHILDREN. (Jap.) Takatsu, T. (Tokyo U. Sch. Med., Japan). Nippon Shonika Gakkai Zasshi (Acta Paediat. Jap.) 67(8):36-37, 1963.

A more detailed account of the paper abstracted as CRA 1(4):#758, 1963.

64-2003 SMOKING HABITS IN LUNG-CANCER PROBAND FAMILIES AND COMPARABLE CONTROL FAMILIES. (E.) Tokuhata, G. K. (St. Jude Res. Hosp., Memphis, Tenn.). J. Nat. Cancer Inst. 31(5):1153-1171, 1963.

The pattern of the familial smoking behavior was analyzed and compared between parents, siblings, and children of 270 lung cancer probands and the counterparts of 270 controls selected within the same community. With respect to cigarette smoking among the index subjects the following were found to be related to lung cancer: (1) smoking at

young ages; (2) the amount of daily smoking (one pack or more); (3) the duration of smoking (40 yr. or more). Three different aspects of cigarette smoking among the relatives were analyzed with the following results: (1) The relatives of the lung cancer probands are more likely to be smokers than those of the controls. (2) About 40% of the case relatives are smokers regardless of the smoking status of the probands; in contrast, smokers comprise 40% of those control relatives whose index subjects are smokers, as compared with 30% of those control relatives whose index subjects are nonsmokers. (3) In both proband and control families, children are more likely to be smokers if their parents are smokers. The results of these analyses do not seem to support R. A. Fisher's "common genotype" hypothesis regarding lung cancer and smoking behavior. (See also CRA 1(1):128, 1963.)

64-2004 TYPES OF TUMORS FOUND BY FEDERAL MEAT INSPECTORS IN AN EIGHT-YEAR SURVEY. (E.) Brandly, P. J. (US Dept. Agric., Beltsville, Md.) and G. Migaki. Ann. N.Y. Acad. Sci. 108(Art. 3):872-879, 1963.

Statistics are presented on the annual slaughter in USDA inspected establishments and condemnations for neoplasms for the fiscal yr. 1955 through 1962. For the yr. 1962 total slaughter for cattle, swine, sheep (millions); horses and goats (thousands), was, resp.: 25.2, 67.1, 14.7; 53.8, 103.5. The number condemned for neoplasms (per 100,000, based on postmortems) was, for the same species: 44.1, 3.40, 1.52, 79.9 and 1.35. Additional numbers of cattle, swine, sheep and horses had body parts condemned because of neoplasms: these were (per 100,000), resp., 244, 0.61, 0.03 and 1.86. In cattle the antemortem rate of condemnation was 2.98. Sheep are generally believed to be relatively free from neoplastic diseases; however, about 95% of sheep slaughtered are lambs. Detailed information for the same years is given on the incidence of epithelioma of the eye for cattle (excluding calves). The rate per 100,000 for 1962 was 323.3. Thus condemnations for epithelioma constitute about 88% of all condemnations for tumors in cattle or 84% of the condemnations for tumors in all species. Presented in tabular form is the microscopic classification of the first 1000 neoplasms submitted to the Biological Sciences Laboratories and received from 1954 to 1959.

64-2005 EPIDEMIOLOGIC STUDIES ON URINARY BLADDER TUMORS IN TURKISH CATTLE. (E.) Pamukcu, A. M. (Dept. Pathol. Anat., Sch. Veterin. Med., U. Ankara, Turkey). Ann. N.Y. Acad. Sci. 108(Art. 3):938-947, 1963.

An epidemiological study and review (41 references) is presented on a type of urinary bladder tumor in cattle which has become closely associated with a syndrome referred to as enzootic

hematuria. While the disease has occurred in most countries of the world, it is usually confined to fairly well defined areas, often quite small. It occurs chiefly in upland areas. It is often associated with poor farm lands. All the usual breeds of cattle, aged 4-12 yr. are chiefly affected. It is rare in young animals and heifers do not develop the disease until after calving. The disease affects the water buffalo in Turkey, Formosa and Indonesia. Males are affected as frequently as females. Within an endemic area, some farms never show active cases. The etiology is not fully understood. Preliminary studies suggest that a fibropapilloma agent is present in the spontaneous bovine urinary bladder tumors.

64-2006 INCIDENCE OF ACUTE MYELOID AND LYMPHATIC LEUKEMIA IN JAPAN. (Jap.) Wakisaka, Y. (Dept. Intern. Med., Kyoto U. Sch. Med., Japan). Acta Haemat. Jap. 26(1):148-149, 1963.

A statistical study is presented of a total of 1,087 cases of leukemia collected from 12 medical school hospitals throughout the country during the past 5 yr. Acute leukemia comprised 67.8% of the cases, with the highest incidence in the age group under 14. Acute lymphatic leukemia showed a tendency to decrease in the older age groups. In terms of geographic distribution, the lowest incidence of acute leukemia (except monocytic) was in areas of Shikoku and Chyngoku (57.6%). The highest incidence was 79.9% in Hokuriku and Chyubu. The lowest incidence of lymphatic leukemia was 3.5% in Chyubu and Hokuriku and the highest was 14.4% in Chyngoku and Shikoku. The incidence of chronic lymphatic leukemia was much lower in all areas studied and none occurred in the Tohoku area. The highest incidence of monocytic leukemia was 18.8% in Chyngoku and Shikoku; the lowest was 2.6% in Chyubu and Hokuriku. However, these geographic differences in the incidence of leukemia are not entirely comparable because some differences exist in the criteria for the diagnosis of the disease in different areas and also in some places some pts. were handled on an ambulatory basis while others were treated only in the hospital.

64-2007 STUDIES ON CHORIOCARCINOMA FROM 88 PATIENTS ADMITTED TO THE PHILIPPINE GENERAL HOSPITAL FROM 1950-1961. (E.) Acosta-Sison, H. (Dept. Obstet., U. Philippines Coll. Med., Quezon City). J. Philipp. Med. Assn. 39(7):560-565, 1963.

See CRA 1(2):#319, 1963.

64-2008 INFLUENCE OF SMOKING ON MORTALITY FROM VARIOUS DISEASES IN SCOTLAND AND IN ENGLAND AND WALES. AN ANALYSIS BY COHORTS. (E.) Crofton, E. (Dept. Resp. Dis. Tubercul., U. Edinburgh, Scotland) and J. Crofton. Brit. Med. J. 2:1161-1164, 1963.

The male:female ratios of death rates at various ages have been analyzed in 10-year cohorts (starting in 1866) and mortality compared in Scotland and in England and Wales. The rise in the male:female ratio of death rates in certain diseases probably connected with cigarette smoking occurred earlier, and to a greater extent, in England and Wales than Scotland. This is clear-cut in the case of bronchitis, carcinoma of the lung, and respiratory tuberculosis. It is probable in ischemic heart disease and possible in peptic ulcer, the influence of both of these diseases being confined to middle age. In pneumonia the position is uncertain, the picture being confused by the introduction of chemotherapy; no association was seen with cerebrovascular accidents. The recent rise in male bronchitis death rate (particularly in the younger age-groups, 45-64) may be partly due to a late smoking effect.

64-2009 VITAL STATISTICS OF THE UNITED STATES. 1960. (E.) U.S. Dept. Health, Education and Welfare. Public Health Serv. Vital Statis. U.S. 2(Pt. A.):427 pp., 1963.

Mortality from neoplasms in the U.S. is treated in section 1, "Mortality Analysis and Summary". In 1960, death rates (per 100,000) for neoplasms was second in rank for white males, white females and nonwhite males (166.1, 139.8 and 134.1, resp.); it was third for nonwhite females (109.8). It is treated in more detail in section 5, "General Mortality Tables". Four tables deal with deaths from 255 selected causes: these deal with analysis by month; by specified race and sex; by age, race, and sex; and by color and sex (U.S. and each state). Deaths and death rates for 59 selected causes are also dealt with by age, color, and sex.

64-2010 MONTHLY VITAL STATISTICS REPORT. PROVISIONAL STATISTICS. (E.) U.S. Dept. Health, Education and Welfare. Public Health Serv. Monthly Vital Statis. Rep. 11(13): 3-39, 1963.

In 1962, malignant neoplasms caused 16% of all deaths, compared to 6% in 1920. The rate of death due to malignant neoplasms was 149.1/100,000 population, differing by less than 2% from the rates for the 7 preceding yr. The death rates for malignant neoplasms of buccal cavity and pharynx, of breast, of urinary organs, and of other unspecified sites have remained fairly stable in this 7-yr. period; those of digestive organs and peritoneum, not specified as secondary, and of genital organs show slow declines; those of the respiratory system increased in 1962 by 3.5% over 1961. For this last group, the rate of increase from 1930 to 1962 is about 7%/yr. The death rates (per 100,000) for leukemia and leukemia show a gradual increase from 6.3 in 1953 to 7.2 in 1962; and for lymphosarcoma and other

neoplasms of lymphatic and hematopoietic tissues, from 6.1 in 1953 to 7.7 in 1962.

64-2011 SOME ASPECTS OF THE CORRELATION BETWEEN SMOKING OF TOBACCO AND CANCER OF THE LARYNX. (It.) Carfagni, G. (Inst. Clin. Otorhinolaryng., U. Rome) and D. Celestino. Valsalva 39(4):173-181, 1963.

Among 535 male pts. with cancer of the larynx seen at the E.N.T. clinic of Rome during the last 5 yr. only 2% were nonsmokers, while smokers of more than 10 cigarettes/day comprised 82% of the cases. The median age of onset for nonsmokers was 61 yr. while it was about 53 yr. for heavy smokers (more than 40 cigarettes per day). The author states that there was a proportional relationship between the number of cigarettes smoked and the percentage of individuals presenting vestibulo-epiglottic localizations while the number with circumscribed cancer of the vocal cords was greater among the heavy smokers.

64-2012 CLINICAL AND STATISTICAL CONSIDERATIONS IN CANCER OF THE LUNG. (It.) Valdagni, C. (S. Lorenzo Civil Hosp., Trento, Italy) and M. Pietrojusti. Minerva Radiol. 8(10):394-400, 1963.

In a series of 400 pts. referred for therapy to the Centro Tumori di Borgo Valsugana between 1953 and 1961 there were 356 men and 44 women (ratio 8:1). The median ages were 55.0 and 54.2 yr., resp. As to residence, 270 (67.5%) were from urban areas and 130 came from rural areas; 17% were farmers. Among the 44 females who had cancer of the lung 93.2% were nonsmokers while among males 45% were heavy smokers (27% in a control series) and 37% were moderate smokers. The parents of 15% of the pts. had a history of cancer, compared to 5.2% in controls. There was a history of some previous lung disease in 41.5%, compared to 17% in the control series. As to the tumors, 56% were adenocarcinomas, 11% epitheliomas, 16.3% sarcomas, 0.5% microcytomas, and 16.3% were without histological diagnosis. Metastases were seen in 52.7% of the cases (more than half of these were of the lymph nodes).

64-2013 MULTIPLE CUTANEOUS EPITHELIOMATOSIS, ARISING 20 YEARS LATER ON CHRONIC ARSENICAL HYPERKERATOTIC LESIONS IN A VINTNER IN BEAUJOLAIS. (Fr., Abstract) Tolot, F. Gauthier, R. Soubrier, J.-R. Bresson and J. Réty. Presse Med. 71(43):2059, 1963.

Multiple cutaneous epidermoid cancers due to multifocal degeneration of hyperkeratotic lesions were observed in a vintner who 20 yr. earlier suffered a severe, subacute arsenic poisoning; this was presumed to be due to the ingestion of grape products from vines where copper arsenate had been used. Chronic dermal lesions had remained,

although there was no further exposure to arsenic. Arsenic values in the urine (before and after treatment with BAL), hair and tumors were normal.

64-2014 ATMOSPHERIC POLLUTION AND BRONCHO-PULMONARY DISEASES. (Fr.)

Gernez-Rieux, C. (A. Calmette Thoracic Hosp., Lille, France) and C. Voisin. Gaz. Med. France 70(20):2983-2991, 1963.

In a general review of all principal broncho-pulmonary diseases, figures are given in which the incidence (per 100,000) of primary broncho-pulmonary cancer for the male population in France increased from 14.3 in 1950 to 29.1 in 1960. The highest incidences for men over 30 yr. of age in the period 1955-1959 were found in the departments of Moselle (61.7), Seine (54.4), Haut Rhin (53.5), Bouches-du-Rhone (52.2), Meurthe-et-Moselle (52.2), and Nord (48.3). The above are the most industrialized areas of the country, where the level of air pollutants could be considered the highest. In rural departments the incidence was much lower (i.e., Vendee (14.9); Aveyron (14.3); Lozere (6.5)).

64-2015 ROLE OF THE HEREDITARY FACTORS IN THE HUMAN LEUKEMIC ETIOLOGY (FAMILIAL LEUKEMIA). (Rus.) Akkerman, V. V. (Leningrad Blood Transf. Inst., USSR). Probl. Gemat. (8):3-8, 1963.

A review (10 references) is presented of the occurrence of familial leukemia involving 96 families and 229 pts. observed between 1953-1958: included are 5 of the author's cases which are presented in detail. Males numbered 113; sex was not determined in 41 cases. As regards the number of members within a family affected, in 3/96 families, there were 2; in 14/96, 3; in 19/96, 4; and 4/96, 5 or 6. In 58/96 families siblings or first cousins were involved; in 20 families one parent and an offspring were involved; in 12 families the disease was present in 4 generations. One type (chiefly acute leukemia) was found in 67/85 families studied; mixed type (mainly chronic myeloid) occurred in 18 families. Where studied, the time interval between onset of disease in individuals within the same family was less than 1 yr. in 33 families and 1-5 yr. in 31 families. Hereditary factors in etiology were suggested by incidence in towns, where acute forms prevailed.

64-2016 FAMILIAL CANCERS OF THE DIGESTIVE TRACT. (Fr.) Dubarry, J.-J. (Clin.

Digest. Dis., Saint-Andre Hosp., U. Bordeaux, France), J.-P. Bernard and Y. Auché. Gaz. Med. France 70(21):3195-3202, 1963.

Cited are 7 instances in the authors' own practices (4 published previously) of cancer of the g.i. tract occurring in more than one member of the same immediate family: (1) gastric cancers in 5/6 siblings; (2) colonic cancers in a mother and son; (3) gastric cancers in both parents, a colonic cancer in the son; (4) gastric cancers in both parents and a daughter; (5) rectal cancer in the father, cecal cancer in a daughter, and a gastric cancer in a son; (6) gastric cancer in a father and 2 sons; (7) rectal cancer in a mother and son. The authors conclude that an hereditary predisposition to cancers of the g.i. tract may exist in certain families, although the phenomenon does not occur frequently.

64-2017 CARCINOMA OF THE ENDOMETRIUM. ETIOLOGY, PATHOLOGIC ANATOMY, FREQUENCY. (Sp.) Francini, M. A. (Palace Maternity Conception, Caracas). Rev. Obstet. Ginec. Venez. 23(2):355-371, 1963.

In an analysis of 29,500 histological examinations and of 3918 biopsies and curettages of the endometrium made during the period 1957-1961 in 3 Caracas hospitals, it was found that 22.9% showed endometrial hyperplasia, about 18% showed cancer of the cervix and 1.22% cancer of the endometrium. Contrary to statistics from other countries the ratio of endometrial to cervical cancer was 1:15.

64-2018 SKIN CANCER AT THE SITE OF CHRONIC ULCERS RELATED TO GUNSHOT WOUNDS. (Rus.) Petrov, V. I. Vestn. Khir. Grekov 91(9):110-111, 1963.

Successful surgery was performed on 5 pts. with planocellular keratotic skin cancer which had developed from gunshot wounds. Two cases are presented in detail where the gunshot wounds occurred 15 and 41 yr. prior to diagnosis. Another case presented in detail stemmed from frost-bite which occurred 17 yr. before diagnosis.

64-2019 MONGOLISM, OTHER CONGENITAL MALFORMATIONS AND CANCERS AMONG BROTHERS AND SISTERS OF LEUKEMIC CHILDREN. (Fr.) Editorial. Concours Med. 85(46):6203-6206, 1963.

A summary of the paper abstracted as CRA 1(2):#286, 1963.

See also abstract nos.: 1853, 1865, 1866

MISCELLANEOUS

- 64-2020 ACUTE LEUKAEMIA IN AN XO/XXX MOSAIC.
(E.) Lewis, F. J. W. (Southmead Hosp.,
England), R. H. Poulding and R. D. Eastham.
Lancet 2:306, 1963.

Cell cultures were made from the blood and marrow of a 64-year-old woman with acute myeloblastic leukemia. Cells with 45 chromosomes contained 22 pairs of autosomes and sex chromosomes XO. Cells with 47 chromosomes contained 22 pairs of autosomes and sex chromosomes XXX. A sample of 100 buccal cells showed the following distribution of numbers of Barr bodies: none, 28%; 1, 35%; 2, 34%; 3, 3%. The pt. gave no indication of mental subnormality, and had borne 3 sons who are said to be normal, alive and well but who were not investigated.

- 64-2021 ANTIGENIC DIFFERENCES BETWEEN NORMAL AND LEUKEMIC TISSUES. (E.) Korosteleva, V. S. (D.I. Ivanovskii Inst. Virol. AMN SSSR, Moscow) and P. N. Kosyakov. Biull. Eksp. Biol. Med. (Eng.) 53(4):452-455, 1963.

The sera of rabbits inj. with spleen extracts from a leukemic pt. showed a high titer of complement fixing (c.f.) antibodies to both normal and leukemic spleen, and the sera gave a non-specific fixation at a lower titer, with antigens from normal liver. When antisera from leukocytes of either of 2 leukemic pts. were adsorbed on formalin-treated normal tissues, equally high c.f. titers were observed to normal and leukemic leukocytes. The adsorbed antisera contained no antibodies to normal erythrocytes or normal liver but gave a weak positive reaction with normal spleen antigens.

- 64-2022 ON THE NATURE OF CONDYLOMA ACUMINATUM OF THE PENIS. (Rus.) Shabad, A. L. (Dept. Urol., Centl. Inst. Postgrad. Med., Moscow). Vestn. Derm. Vener. 37(9):53-56, 1963.

In a report on an investigation of both hospitalized and outpatients, the author states that condyloma acuminatum of the penis has the histological structure of papilloma with some specific features of its own. In lingering cases, neglected condyloma of the penis may undergo malignant change. It should be regarded as a true tumor, considered as potentially a precancerous condition and be called virus papilloma of the penis.

- 64-2023 CONNECTIVE TISSUE SYNDROMES ASSOCIATED WITH CARCINOMA. (E.) MacKenzie, A. H. (Dept. Rheum. Dis., Cleveland Clin. Found., Ohio) and A. L. Scherbel. Geriatrics 18(10):745-753, 1963.

Of 77 pts. with connective tissue syndromes associated with carcinoma, 19 had hypertrophic

osteoarthropathy, 18 rheumatoid arthritis and 13 had dermatomyositis. As regards others with connective tissue disease (CTD), 2 had disseminated lupus erythematosus; 2 had polymyositis; 4 had rheumatoid arthritis (stage II or III) of long duration; 11 had acute monoarthritis, migratory tenosynovitis, and localized acute transient periarticular inflammation; 7 had a severe, rather disabling fibrositic syndrome; 1 pt. showed rapidly progressing systemic sclerosis. As regards the tumors 72/77 were carcinomas. Among the latter, the chief sites involved were: bronchus 18, prostate 15, breast 13, colon-rectum 4, and 2 each stomach, urinary bladder, pancreas, ovary, kidney and larynx. While rigorous proof of a causal relationship is not yet attainable, the following relationships are of interest: (1) Onset of CTD took place within a reasonable time interval of discovery of tumor in 50 of 61 pts. (2) CTD was promptly abolished following successful control of the tumor in 25/30 pts. (3) CTD recurred in 5/10 when the tumor reappeared.

- 64-2024 SMOKING AND THE HEALTH OF OLDER MEN. II. SMOKING AND VENTILATORY FUNCTION. (E.) Weiss, W. (Women's Med. Coll. Penna., Philadelphia), K. R. Boucot, D. A. Cooper and W. J. Carnahan. Arch. Environ. Health (Chicago) 7(5):538-547, 1963.

Among 294 men aged 50-69 yr. reporting routinely for a checkup to the Philadelphia Pulmonary Neoplasm Research Project the highest percentage of ventilatory abnormalities (as measured by vital capacity, 1- and 3-second forced expiratory volume, and maximal expiratory flow rate) was found in heavy cigarette smokers, in cigarette smokers of long duration, and in cigarette smokers with abnormal photofluorograms and symptoms. It is suggested these findings represent chronic bronchial obstruction due to irritative bronchitis. Ex-smokers had ventilatory values intermediate between those of nonsmokers and those of current smokers.

- 64-2025 CYTOGENETIC EVIDENCE OF CLONAL PROLIFERATION IN PRIMARY RETICULAR NEOPLASMS. (E.) Ford, C. E. (Med. Res. Coun., Radiobiol. Res. Unit, Harwell, Didcot, Berkshire, England) and C. M. Clarke. Canad. Cancer Conf. 5:129-146, 1963.

In sublethally irradiated mice which are undergoing regeneration, a study of the karyotypes of bone marrow cells revealed that the same set of abnormal chromosomes may recur repeatedly in different cells of the same animal. Extensive studies were made of cells from a reticulosarcoma found in an unirradiated 35-month-old hamster. Among 402 cells examined, only 3 failed to show a set of 3 marker chromosomes; among 242 bone marrow cells only 1 such karyotype was found while none were seen among 98 spleen cells. A detailed

study was made of karyotypes seen in cultures of cells from a sternal biopsy of a pt. with acute leukemia. Among cells with 47 and 48 chromosomes, 8 different cell types were found. In a direct bone marrow examination of another pt. with chronic myeloid leukemia, of 15 cells analyzed, only 1 was doubtfully normal. Probably all the remainder contained the Ph¹ together with another striking "marker". These 2 chromosomes were not found in cultures made during a period of remission following treatment with Myleran. Later when blasts cells appeared, new cultures showed not only the reappearance of these 2 chromosomes but at least 3 further changes. In an extensive discussion the authors believe these results are best explained on the basis of clonal proliferation as opposed to an independent origin. The possible relation of this clonal development to changes in malignancy is also discussed.

64-2026 INCIDENCE OF SPONTANEOUS HEPATOMAS IN HEPATECTOMIZED C 3H/Mza MALE MICE.

(E.) Echave Llanos, J. M. (Fac. Med. Sci., Nat. Cuyo, Mendoza, Argentina) and I. E. Saffe. *Naturwissenschaften* 50(19):619, 1963.

Incidence of spontaneous hepatomas in untreated mice was 21.1% (18/85); after removal of the median and left lobes of the liver, 13.7% (11/80); after a second hepatectomy 12 mo. later at which time the left lobe was removed, 7.1% (5/70). Thus the decreased incidence is related to the number of hepatectomies and not to the removal of specific lobes. It is believed that the cells resulting from regenerative processes show increased resistance to the development of tumors.

64-2027 AN ABNORMAL CHROMOSOMAL PATTERN IN MYELOMATOSIS. (E.) Lewis, F. J. W. (Dept. Path., Southmead Hosp., Bristol, England), L. Fraser and M. MacTaggart. *Lancet* 2: 13-1015, 1963.

Case of myelomatosis in a 76-year-old woman is presented. The chromosomes in cells cultured from the sternal bone marrow showed a grouping around the normal number and an associated group within the range of 50-56. Other chromosomal abnormalities in structure were also seen both in direct non-culture or short-term-culture preparations. (See also CRA 1(4):#771, 1963.)

64-2028 ALTERATION OF VIRULENCE OF MN ASCITES SARCOMA AFTER CONTINUOUS CULTURE IN VITRO. (E.) Takahashi, M. (Dept. Path., Naguchi Sch. Med., Japan). *Gann (Jap. J. Cancer Res.)* 54(3):295-310, 1963.

Ascites sarcoma cells (T strain) maintained by continuous culture *in vitro* (culture line) were markedly less virulent in female mice (measured in terms of median survival time) than when maintained by serial transfers in female mice (animal

line). Inoculation of the culture line allowed female hosts to survive until the tumor cell population was larger than that tolerated by the same hosts inoc. with the animal line. After inoc. into male mice the culture line caused fewer and less extensive metastases than the animal line. The difference between the 2 lines was less conspicuous in females than in males, probably because a reduced histotrophism of the culture line was counteracted by a longer survival time of the female hosts. As regards chromosome constitution, the culture line was hyperdiploid, while the animal line was hypodiploid. The chromosomes of the culture line showed greater morphological variations and the individual chromosomes as well as sets of chromosomes were distinct from those of the animal line. Among possible mechanisms for cytological changes, rearrangement or reconstruction of chromosomal materials was suggested. It was impossible to correlate the alteration of virulence with changes of particular types of chromosomes.

64-2029 INVESTIGATIONS ON CHROMOSOMES IN LEUKEMIC CHILDREN. (E.) Schuler, D. (2nd Dept. Pediat. Med. U., Budapest) and S. Kiss. *Folia Haemat. (Leipzig)* 80(4):419-424, 1963.

In an investigation of karyotypes of the peripheral blood of 5 children (ages 3-9) with acute stem cell leukemia, the chromosome number in 4/5 cases (45 cells examined) was predominantly normal (46), in 1 child, 2/10 cells showed numbers between 41-45. The structure of the chromosomes was normal. It is concluded that chromosome anomalies do not play a part in the development of acute stem cell leukemia of childhood.

64-2030 ABO BLOOD GROUPS AND Rh. ANTIGENS IN PATIENTS WITH CARCINOMA OF THE BREAST. (E.) Torti, R. A. (Washington Hosp. Ctr., D. C.). *Med. Times* 91(12):1167-1168, 1963.

In 529 pts. with breast cancer (including 47 negroes) percentage frequency as to blood group was "O" 48.2, "A" 37.1, "B" 11.3 and "AB" 3.2. Normal values for the U. S. white population is, resp., 45, 41, 10 and 4. For pts. Rh+ frequency was 85.8%, RH- 14.1%; normals 85.1% and 14.9%, resp. None of the differences were statistically significant.

64-2031 THE ASSOCIATION OF MALIGNANT LYMPHOMA WITH SJÖGREN'S SYNDROME. (E.) Bunim, J. J. (NIH, Bethesda) and N. Talal. *Trans. Assn. Am. Physician* 76:45-56, 1963.

A more detailed account of the paper abstracted as CRA 1(4):#749, 1963. The hypothesis is presented and discussed that in Sjögren's syndrome the chronic state of immunologic hyperactivity and the proliferation of immunologically competent cells producing abnormal tissue antibodies,

predispose to development of malignant lymphoma.

64-2032 SQUAMOUS CARCINOMA ASSOCIATED WITH CYSTS OF THE SKIN IN MERINO SHEEP. (E.)

Carne, H. R. (C.S.I.R.O. Anim. Health Lab., Parkville, Victoria, Australia), L. C. Lloyd and H. B. Carter. J. Path. Bact. 86(2):305-315, 1963.

Stratified squamous carcinoma (64 cases) of a previously unreported type arising from the walls of characteristic cysts in wool-bearing areas of the skin developed in 35 sheep of 3 different flocks. Limited data suggests a new case incidence of 0.6-10% in cyst-bearing sheep/yr. Excision usually prevents recurrence but in one sheep up to 16 additional tumors developed. Tumors have also been noted in the periorbital area (2 cases), outer surface of the ear (2 cases) and on the lip (1 case). Cyst formation is thought to be related to a genetically conditioned abnormality of the epidermis leading to a ready detachability of some of its cells by a penetrating grass seed so that they are carried into the dermis, thus representing an abnormal susceptibility to the formation of "implantation dermoids".

64-2033 CARCINOMA OF THE SKIN--A GUIDEPOST TO INTERNAL MALIGNANCY? (E.)

Carpenter, C. L., Jr. (Dept. Med., Tulane U., New Orleans, La.), V. J. Derbes and H. W. Jolly, Jr. J.A.M.A. 186(7):621-623, 1963.

Of 2,433 pts. with skin cancer gathered from the Charity Hospital Tumor Registry, 197 (8%) were found to have an associated malignancy of another organ. Age-adjusted incidence rates tend to further confirm this association. Of the 197 pts. with multiple cancer, skin malignancy was diagnosed first in 127 (64%) of the cases.

64-2034 SPONTANEOUS CANCER IN MICE. (E.)

Hoag, W. G. (Roscoe B. Jackson Mem. Lab., Bar Harbor, Maine). Ann. N. Y. Acad. Sci. 108(Art. 3):805-813, 1963.

A discussion is presented of a number of factors that must be taken into account when evaluating incidence rates of spontaneous cancer in mice. On the basis of data collected over a period of several yr., the incidence (per cent) of lymphatic leukemia, mammary adenocarcinoma and primary lung tumors is given for 13 inbred strains of mice. These are offered as a guide because these rates are subject to change. As an example, over a period of 10 yr. mammary adenocarcinoma occurred in 50% of breeding female DBA/2J mice. Then for 2 yr. the colony suffered a breeding slump and the rate fell to less than 1%. It was felt that the rate was related to the number of litters produced. However, when the breeding problem was corrected by a change in diet and the colony produced 3x as many young to reach a new high in breeding performance, the spontaneous

mammary cancer rate still remained near the zero level. The author believes that studies on spontaneously occurring cancer in inbred mice should be used as strong supplements to a cancer research program. An appendix contains separate selected bibliographies (approx. 575 references) for 49 strains of mice collected during 2 periods: 1940-44 and 1958-62.

64-2035 WHAT IS PRESENTLY KNOWN ABOUT HEPATOMA IN HATCHERY-RAISED RAINBOW TROUT (SALMO

IRIDEUS). (Fr.) Levaditi, J., P. Besse, R. Vibert, J.-C. Guillon and O. Nazimoff. C. R. Acad. Sci. (Paris) 257(10):1739-1741, 1963.

Histologic examination of 42 hepatomas in French, hatchery-raised rainbow trout confirmed earlier descriptions of the same malignancy which occurs in Italy and the U. S. A. All, including the U. S. trout, were descendants of the same progenitors, originally taken from a river in the state of Washington; the European trout were the product of continuous interbreeding of the same line since 1925, with succeeding generations fed on products derived from surplus human food. In addition, two cases of metastases to the myocardium were also seen. Hepatomas were also seen in a wild specimen ("omble chevalier") taken close to the hatchery from which the lake was stocked, and a hatchery-raised 4-year-old "fountain salmon."

64-2036 CANCER ON SCARS. MARJOLIN'S ULCER.

(Sp.) Jonquieres, E. D. L. (Durand Hosp., Buenos Aires) and N. Barrile. Prensa Med. Argent. 50(10):677-680, 1963.

In 4 cases (2 men and 2 women, ages 42-60) grade I and III spinocellular epitheliomas developed on scars (some partially repaired by plastic surgery) which resulted from extensive burns suffered 25-43 yr. earlier. A 52-year-old woman developed a grade II spinocellular epithelioma at the site of the wound inflicted 20 yr. earlier during the course of a cholecystectomy. The wound had suppurated and left a large scar. A 63-year-old man developed a grade I spinocellular epithelioma on the scar remaining from an accident which occurred 45 yr. earlier when his hand was caught in a machine.

64-2037 CLINICAL CONSIDERATIONS ON TWO CASES OF TESTICULAR SEMINOMA ARISING AFTER TRAUMA

(It.) Ragaglia, G. (Inst. General Clin. Surg., U. Pavia, Italy) and F. de Luca. Riv. Pat. Clin. 18(4):187-199, 1963.

A 26-year-old man observed enlargement and hardening of the right testicle 2 days following impact. The testicle was removed 5 mo. later following further enlargement. Histologic examination showed it to be a seminoma. A seminoma was also found in the left testicle of a 54-year-old man 4 mo. after he had suffered trauma to the area.

4-2038 NEW EXPERIMENTAL INVESTIGATIONS ON THE METASTATIC DIFFUSION OF MALIGNANT TUMORS. I.- INTRAVENOUS INJECTIONS OF GUERIN EPI-THELIOMA HOMOGENATES INTO INTACT OR BIOLOGICALLY MODIFIED WISTAR RATS. (Fr.) Driessens, J. (Dept. Biol., Cancer Res. Inst., Lille, France), J. Clay, J. Vanlerenberghe, L. Adenis and J. Quandalle. Bull. Assn. Franc. Cancer 50(2): 83-194, 1963.

When normal Wistar rats (Gif. strain) of both sexes, av. wt. 200 g, received 1-5 i.v. inj. of Guerin carcinoma cells (10,000 cells/inj.) at monthly intervals, 12/56 developed a total of 15 tumors (6 renal, 6 adrenal, 3 pulmonary), while 4/56 were resistant to total inj. of up to 25 million cells. Similar treatment of animals already bearing s.c. inoc. of Guerin carcinoma resulted in active tumor takes in 12/15 (2 renal, 1 adrenal, 1 pulmonary + quiescent conc. of malignant cells in these same areas in 5 of the rats). Retreatment disturbance of systemic or hormonal balance by pneumogastric section or inj. of somatotropic hormone, cortisone, deoxycorticosterone, chlorpromazine did not affect these results, though pretreatment splenectomy increased tumor takes to 17/25 animals, with a total of 38 tumors (2 lymph node, 11 renal, 8 adrenal, and 7 pulmonary). The presence in all of the animals of quiescent conc. of malignant cells appeared to lend support to the idea that a given individual may carry such foci of potential malignancy for long time, while some thus far unidentified, genetic mechanism of defense keeps them "dormant" or "quiescent". (See also CRA 1(9-10):#1803, 1964.)

2039 INFLUENCE OF THYMECTOMY AND SPLENECTOMY ON LEUKEMIOGENESIS AND SURVIVAL IN MICE. (E.) Rudali, G. (Radium Inst., Curie Found., Paris) and P. Jullien. Bull. Assn. Franc. Cancer 50(2):203-218, 1963.

Among thymectomized AkR newborn mice, 149/279 died before weaning and another 114 between the ages of 35 and 160 days. Among the 16 survivors 1 case of lymphatic leukemia was found. All the thymectomized animals which died suffered from an acute atactic syndrome similar to that produced by *Monella typhimurium*. In (AkR x RIII/f)F1 mice, controls showed 1/48 animals with spontaneous lymphocytic leukemia with a latency of 740 days, 1 spontaneous mammary tumor. Among 27 animals thymectomized at birth, none showed spontaneous lymphocytic leukemia, 1/27 had a myeloma, and there were 1 cranial osteoma and 1 rhabdomyosarcoma. The av. survival for this group of animals was 582 days (compared to 800 days for the controls). No tumors were observed in 8 survivors among 22 thymectomized at birth, followed by implantation of thymus tissue obtained from RIII/f newborn mice; av. survival was 609 days. When, following thymectomy, the hybrid animals received bits of AkR thymus tissue, there were 1/27 with thymoid leukemia (latency 423 days), 1 reticulum

cell carcinoma, 2 fibrosarcomas and 2 cranial osteomas (av. survival for this group, 581 days). Injection with passage G extracts (C.R. Acad. Sci. 250:1588-1589, 1960) in controls at birth produced lymphocytic leukemia in 29/32 animals with an av. latency of 220 days. In addition, there were 1 myxosarcoma and 1 osteogenic sarcoma. When the passage G material was inj. in thymectomized animals, there was 1/19 lymphocytic leukemia, (latency, 460 days) but there were 6 reticulum cell sarcomas and 1 s.c. fibroma. Average survival in the latter 2 groups was 220 and 362 days, resp. Splenectomy of AkR or C57Bl mice, at birth or in adulthood, did not alter significantly the incidence of spontaneous leukemias; splenectomy of (AkR x R III/f)F1 mice at birth did not alter the incidence of leukemias induced by inj. of passage G extract.

64-2040 UNUSUALLY HIGH POLYPOIDY IN A HUMAN CANCER. (E.) Sandberg, A. A. (Roswell Park Mem. Inst., Buffalo, N. Y.), T. Ishihara, G. E. Moore and J. W. Pickren. Cancer 16(10): 1246-1254, 1963.

A case is presented of a 60-year-old man with cancer of the sigmoid colon with extreme karyotypic abnormality of cells in the peritoneal fluid. Over 50% of the cells contained 600 or more chromosomes, with some metaphases containing several thousand. In the metaphases examined, very abnormal ring, dicentric and long acrocentric chromosomes were present. Upon culture, the cells of the effusion that survived had mostly the modal number of chromosomes (hypotetraploid).

64-2041 NEOPLASTIC TRANSFORMATIONS IN C3H MOUSE EMBRYONIC TISSUE IN VITRO DETERMINED BY INTRAOCULAR GROWTH. I. CELLS FROM CHEMICALLY DEFINED MEDIUM WITH AND WITHOUT SERUM SUPPLEMENT. (E.) Evans, V. J. (NCI, Bethesda), G. A. Parker and T. B. Dunn. J. Nat. Cancer Inst. 32(1):89-121, 1964.

Tissue from minced C3H mouse embryos was cultured in both chemically defined medium NCTC 109 alone and with 10% horse serum. In the serum-supplemented medium, *in vitro* neoplastic transformations were biologically verified by intraocular and i.m. implants of 3 series of the tissue. Cells of the series 1 cultured for 176 days produced grossly observable growths. Series 2 and 3 required 147 and 124 days, although histologically a fibrosarcoma was obtained from cells of the second series only 121 days *in vitro*. On implantation, cells 117 days *in vitro* in the series 3 failed to produce tumors; apparently an alteration occurred within 1 wk. The ability of cells to produce tumors was preceded by an increased rate of proliferation in cultures. These tumors were composed predominantly of fusiform cells and occasionally had inclusions of cartilage and bone. Because fusiform fibroblastic cells predominated, the tumors were designated fibrosarcomas. The period

between implantation of cells from cultures and appearance of the tumors shortened with increased time in vitro. Several tumor transplants produced rapidly growing fibrosarcomas within 13-145 days. Cultures grown on chemically defined medium NCTC 109 alone have been kept alive in vitro over 19 mo. No progressively growing tumors appeared from a limited number of intraocular implants from these cultures; some early growths were resorbed. Some sections showed small areas of ossification, but no neoplastic areas were observed. The reproducibility of time of occurrence and nature of the response in this study suggests the suitability of the system for pursuing studies of neoplastic transformations in vitro.

64-2042 LONG-TERM TISSUE CULTURE OF NEUROBLASTOMAS. II. MORPHOLOGIC EVIDENCE FOR DIFFERENTIATION AND MATURATION. (E.) Goldstein, M. N. (Cell Biol. Lab., St. Jude Res. Hosp., Memphis, Tenn.), J. A. Burdman and L. J. Journey. J. Nat. Cancer Inst. 32(1):165-199, 1964.

Neuroblastoma cells were obtained from 13 young children and cultured in vitro for periods of 1 wk. to over a yr. All but one of the biopsies contained undifferentiated masses of immature neuroblasts resembling small lymphocytes. Within 5 mo. the neuroblastoma cells underwent maturation and differentiation as evidenced by an increase

in nuclear size, development of a single large nucleolus, accumulation of Nissl RNA substance, the formation of neurofibrils, and hypertrophy of axons. Explantation of a more mature appearing neuroblastoma resulted in the transformation of all the nerve cells into mature ganglion cells within 20 days. The studies in vitro suggests that neuroblastoma may be the result of a biochemical defect which would prevent maturation of the nerve cells or a tumor population whose progeny have the potentialities to differentiate and mature.

64-2043 CYST AND TUMOR OCCURRING IN THE SAME KIDNEY. (E.) Levine, S. R. (Mayo Clin., Rochester, Minn.), J. L. Emmett and L. B. Woolner. Trans. Am. Assn. Genitourin. Surg. 55:118-119, 1963.

Of 1007 surgically explored cases of renal cyst or tumor (545 renal carcinoma, 24 cystic hypernephroma), 10 cases were found in which tumor and cyst coexisted in the same kidney (an incidence of 1% for the whole group or 2.3% of the 438 case of renal cysts. In only 1 of these cases was the tumor close enough to the cysts to be considered a possible etiologic factor in its origin. No case was found in which a tumor occurred inside a simple serous cyst containing clear fluid (transudate).

ERRATA:

1(5):#783, 1963. Line 10, column ii, while the percentages quoted are from the paper, 1.4% and 86% appear correct according to the data.

1(6): 1963. Author Index, page ii, change Rabson, A. S. to Rabson, A. S.

1(6):#1196, 1963. Correct the second author's name to read Phan-Dăn.

1(7):#1391, 1963, 1(8):#1503, 1963, and 1(9-10):#1782, 1964. Change journal volume from 1 to 2.

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration(s)	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health, USA
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit(s)
e.g.	for example	ppm	parts per million
FFU	focus forming unit(s)	pt.(s)	patient(s)
g	gram(s)	RBC	red blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
ID ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution(s)
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit(s)
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose(s)	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

4-2044 CLINICAL ASPECTS AND ETIOLOGY OF
OSTEOSARCOMA. (Ger.) Ott, G. (Surg.
lin., Ruprecht-Karl-U., Heidelberg, Germany)
and P. Ehlers. Med. Welt (38):1907-1915, 1963.

Cancer, the cause of 1 out of every 30 deaths at the turn of the century, now causes 1 out of every 5 deaths in W. Germany. This increase is attributable not only to the present doubled life expectancy, but also to the vast increase in environmental carcinogens. Carcinomas of the epithelial tissues comprise 85% of all malignancies although these tissues constitute only 17.5% of the body; sarcomas account for only 6% of all malignancies although mesenchymal tissues comprise 82.5% of the body. In 1957, W. German deaths from malignant bone tumors were 2.1/100,000 inhabitants, or 1% of all cancer deaths. Among all osteosarcomas first treated between 1943 and 1961 61.1% were osteogenic, 19.1% myelogenic, 9% parosteal and 9.9% other types. Osteosarcomas, especially the osteogenic type, occur preferentially in areas and at times of most active and rapid growth: about 40% in the distal humerus and proximal tibia and most frequently at ages 11-20 yr. Mean age of onset (which had remained fairly stable between 1925 and 1959 for soft tissue sarcomas and for malignant melanomas) for osteosarcomas during 1950-1959 dropped from 21.1 yr. to 26.4 yr., an 8 yr. drop. This earlier appearance of osteosarcoma is attributed to uptake in growing bones of strontium 90, accumulated from atom bomb test fallout, by inhalation, food and water intake and even by fetal uptake through the placenta). The much publicized safety of small doses of radioactivity is erroneous. Other etiologic factors discussed include trauma, benign tumors and pre-sarcomatous bone diseases such as chronic osteomyelitis and Paget's disease; deformed; implanted foreign bodies such as fracture pegs (and a case of bone marrow transplantation); occupational exposure, such as in radiologists and radium watch dial painters; and carcinogenic factors, such as irradiation of bones and admin. of the radioactive Peteosthor (a fluorescent derivative containing thorium X) to children with bone TB. (32 references)

4-2045 THE BIOCHEMISTRY OF BLADDER CANCER.
(E.) Boyland, E. (Chester Beatty Res.
Inst., U. London, England). Publ. No. 516
American Lecture Series. Karnofsky, D. A. (Ed.).
C. Thomas Publ., Springfield, Ill., 95 pp.,
1963.

The history of bladder carcinogenesis including discovery of occupational bladder cancers, and other environmental effects involved in bladder carcinogenesis (smoking, Bilharzia infection) is reviewed critically. Also reported are studies of experimental induction in animals, including hydrazine induction in dogs, induction by methoxymines in other species, and by local applications

of various carcinogens. The metabolism of aniline, 2-acetamidofluorene, 4-aminobiphenyl and 2-naphthylamine is treated at some length as are possible biochemical mechanisms for localization of bladder carcinogens by arylhydroxylamines and o-amino-phenols, by excreted metabolites, and by enzymatic hydrolysis in urine. Some data collected by J. H. Davies shows abnormally high β -glucuronidase activity in the urine of pts. with very advanced bladder cancer. The results taken as a whole do not indicate that the high β -glucuronidase excretion necessarily precedes development of cancer, but should, however, be sufficient to release carcinogenic o-aminophenols or arylhydroxylamines from their inert glucuronides. Among various theories of carcinogenesis by aromatic amine metabolites discussed are deletion of suppressors by carcinogens and combination with tissue components. Also treated are the effects of metabolites of carcinogenic polycyclic hydrocarbons, 2-acetamidofluorene and a comparison of arylhydroxylamines and alkylating agents. One chapter is devoted to endogenous carcinogens (metabolism of tryptophan). (Approx. 235 references)

64-2046 EXPERIMENTAL LEUKEMIA. (Heb.)
Trainin, N. (Dept. Exp. Biol., Weizmann
Inst., Rehovoth, Israel). Dapim Refuim 22(1-2):
52-61, 1963.

A review is presented of virus-induced experimental leukemia in poultry and mice and leukemia induced in mice by polycyclic hydrocarbons, estrogens and by ionizing radiation. Recent investigations indicate that in some strains of mice with a high incidence of spontaneous leukemia a viral agent may be involved. (46 references)

64-2047 EXPERIMENTAL ASPECTS OF TOBACCO
CARCINOGENESIS. (E.) Wynder, E. L.
(Sloan-Kettering Inst., New York) and D. Hoffman.
Dis. Chest 44(4):337-344, 1963.

For an earlier report, see CRA 1(9-10):#1633, 1964. Some additional material is presented on the effect of filter materials on the composition of tobacco smoke (see also CRA 1(9-10):#1694, 1964). Bibliography available from the authors.

64-2048 MALIGNANT CHANGE IN PRE-EXISTING SKIN
LESIONS. (E.) Editorial. J. Indian
Med. Assn. 41(6):317-319, 1963.

A review and discussion is presented concerning various preexisting skin lesions and the relative incidence of malignant change. Most stress is laid on malignant change in healed scars and cancerous change in chronic nonneoplastic skin lesions including chronic ulcers of various origins, with or without history of trauma. (9 references)

- 64-2049 THE EPIDEMIOLOGY OF BREAST CANCER. (E.) Lilienfeld, A. M. (Johns Hopkins Sch. Hyg. Public Health, Baltimore, Md.). Cancer Res. 23(9):1503-1513, 1963.

Available data on the epidemiology of breast cancer are reviewed, with the conclusion that the effect of hormonal factors need further and more precise study. With respect to female breast cancer four types of study are suggested: (1) a community-wide study of the characteristics of female breast cancer pts. as compared with a probability sample of the general population; (2) a well controlled intensive study of the family members of pts.; (3) a series of prospective studies on specific types of relationships such as artificial menopause, benign breast conditions, and nursing habits; (4) a study of the observed international differences, particularly with respect to Japan and Finland. (45 references)

- 64-2050 HORMONAL DISTURBANCES AND TUMORIGENESIS: AN INVESTIGATOR'S POINT OF VIEW. (Sp.) Lipschutz, A. (Inst. Exp. Med., Nat. Dept. Health, Santiago, Chile). Rev. Confed. Med. Panamericana 10(2):61-67, 1963.

A general discussion is presented of hormonal homeostasis with particular reference to the formation of ovarian tumors when ovarian tissues are transplanted into animals of different species or into other organs. (16 references)

- 64-2051 CARCINOGENIC IMPLICATIONS ON INHALED POLLUTANTS. (E.) Nelson, N. (Inst. Indust. Med., New York U. Med. Ctr., N. Y.). Arch. Environ. Health (Chicago) 8(1):100-104, 1964.

In a general review of the external factors which might possibly induce lung tumors, the action of several well known carcinogens is discussed. Included are: viruses (specific and nonspecific), radiation, chromium, ruthenium¹⁰⁶, existence of scars and previous respiratory disease. (14 references)

- 64-2052 THE NUCLEIC ACIDS OF VIRUSES AS REVEALED BY THEIR REACTIONS WITH FLUOROCHROME ACRIDINE ORANGE. (E.) Mayor, H. D. (Dept. Virol. Epidemiol., Baylor U. Coll. Med., Houston, Tex.). Internatl. Rev. Exp. Pathol. 2:1-45, 1963.

Reviewed are studies of virus localization and replication using acridine orange as a specific stain or as a vital dye. The use of acridine orange has allowed documentation of both a nuclear and a cytoplasmic phase for SV40 virus in green monkey tissue cultures, with demonstration that the cytoplasmic phase is established before cytopathic effects. In these cultures during the nuclear phase of the viral replication

cycle the cellular chromatin is pushed to the periphery. The cytoplasmic phase found in the green monkey cultures is not observed in rhesus monkey tissue cultures, where the association remains nuclear, and cytoplasmic vacuolation is seldom encountered. Numerous other examples of the replication of DNA and RNA viruses are given and there is a discussion of the photodynamic inactivation of various viruses by the fluoro-chrome. (See also CRA 1(2):#265, 1963.) (93 references)

- 64-2053 THE CARCINOGENIC ACTIVITY OF IRON COMPLEXES. (Por.) Boerman, A. J. Rev. Brasil. Cir. 46(2):113-114, 1963.

In answer to a query, the author reviews the evidence dealing with iron-dextran and other macromolecular complexes and concludes that these compounds have shown carcinogenic properties when admin. to some species of experimental animals. (See also CRA 1(8):#1464, 1963.) (8 references)

- 64-2054 COMPARATIVE PATHOLOGY OF HUMAN AND CANINE CANCER. (E.) Mulligan, R. M. (Dept. Path., U. Colorado Sch. Med., Denver). Ann. N.Y. Acad. Sci. 108(Art. 3):642-690, 1963.

A review and discussion is presented of the pathogenesis and incidence of cancer in man and dog. Detailed discussions deal with the relative incidence of different types of cancer and cancer in various sites, and the influence of physiologic factors such as senescence. Sites often affected in both species include breasts, skin, ovaries, hematopoietic system, and the peripheral nervous system. Cancers common in man but uncommon (range of 0.01-0.2%) in the dog include those of the large intestine, stomach, prostate, pancreas, lungs, cervix and fundus uteri, urinary bladder, biliary passages, central nervous system, esophagus, kidneys, larynx, lips, and tongue. Cancers common in the dog but uncommon in man include those of soft parts, testes, and anal and other apocrine glands. (Approx. 240 references)

- 64-2055 THE RELATIONSHIP BETWEEN X-RAY IRRADIATION AND LEUKEMIA. (Jap.) Miyata, H. (Dept. Int. Med., Nihon Red Cross Centl. Hosp., Tokyo, Japan). Rinsho Ketsueki (Jap. J. Clin. Hemat.) 4(1):1-17, 1963.

A review is presented of the occurrence of leukemia in relation to atom bomb exposure, and exposure to X-irradiation and radioisotopes. (107 references)

- 64-2056 VIRAL TUMORS OF CHICKENS WITH PARTICULAR REFERENCE TO THE LEUKOSIS COMPLEX. (E.) Beard, J. W. (Dept. Surg., Duke U. Med. Ctr., Durham, N. C.). Ann. N.Y. Acad. Sci. 108(Art. 3):1057-1085, 1963.

A comprehensive review and discussion of the occurrence, factors influencing transmission, and characteristics of virus-induced chicken tumors. For other papers in this series see CRA 1(3): #462, #489, #490; *ibid.* (4):#615, #716; *ibid.* (5):#787, #926, #927, #946, 1963 and *ibid.* (9-10): #1747, #1748, 1964. The author suggests that the biochemical basis for the selectivity of interaction between a given virus strain and certain tissues may be related to specific aspects of the constitution of the virus which are concerned, at least in part, with characteristics of the RNA. (85 references)

64-2057 THE THEORETICAL INTERPRETATION OF THE PROBLEMS OF CANCER. PART I. (Ger.) Graffi, A. (Inst. Exp. Cancer Res., German Acad. Sci. Berlin, Berlin-Buch). *Hippokrates* 34(23): 923-930, 1963.

Presented is a brief outline of current theories concerning the nature of the neoplastic cell and the possible roles of chemical agents, viruses, endogenous carcinogens, radiation, mutational changes in genes or cytoplasm, and/or loss of cytoplasmic structural proteins in carcinogenesis. In a 2nd and 3rd part, to follow, each of these subjects will be dealt with at some length. (No references)

64-2058 VIRAL THEORY OF MALIGNANT TUMOR FORMATION IN THE LIGHT OF THE MOST RECENT RESEARCH. (Hung.) Melczer, M. (Dermatol. Dept., J. Pesc, Hungary). *Orv. Hetil.* 104(29):1360-1363, 1963.

In connection with the possible viral origin of cancer, a discussion of experimental findings and their possible implications for clinical oncology are presented. The author feels it will not be long until the viral origin of one or another human malignancy is established. (69 references)

64-2059 VIRUSES, NUCLEIC ACIDS, AND CANCER. A COLLECTION OF PAPERS PRESENTED AT THE SEVENTEENTH ANNUAL SYMPOSIUM ON FUNDAMENTAL CANCER RESEARCH, 1963. (E.) U. Texas M.D. Anderson Hosp. Tumor Inst. Williams and Wilkins Co., Illus., 659 pp., 1963.

This report on recent advances on viruses includes both nontumorigenic as well as tumorigenic viruses. The presentations are well illustrated with line drawings and excellent photographs, are accompanied by bibliographies after each chapter, and include discussions and occasional addenda. Among 9 papers on structure, 2 of more direct interest to oncologists are on that of mammary tumor virus (MTA; Bittner) and of leukemia (Gross) by L. Dmochowski, C. E. Grey, F. Padgett and A. Sykes and on virus particles of mouse

lymphoma and mammary carcinoma by R. Kinoshita and T. Kakefuda. Relative to studies on virus replication and the biochemistry of infected cells, there is included a study of the Bittner virus by D. H. Moore and M. J. Lyons. Among papers on viral nucleic acid is a study of the properties of polyoma virus DNA by R. Dulbecco. A section on avian viruses and neoplasia includes: biological and structural properties of Rous sarcoma virus (R. J. C. Harris); studies on biological, biochemical, and biophysical properties (J. W. Beard, et al.); infection of cultures by avian myeloblastosis virus (AMV) (P. K. Vogt); and induction of differentiation in target cells (*in vitro*) by AMV (M. A. Baluda, J. E. Goetz and S. Ohno). The Bertner Foundation Lecture, by L. Gross, is on the properties of a virus from leukemic mice which induces various forms of leukemia and lymphomas in mice and rats. The section on interferon includes a study by A. C. Allison on interference and interferon in relation to tumor viruses and tumor cells. Included in the section on biological aspects of tumor induction are papers by M. Stoker (polyoma virus and hamster fibroblasts); K. B. DeOme (MTV and mouse mammary noduligenesis and tumorigenesis); and H. Rubin and H. Hanafusa (significance of absence of infectious virus in virus-induced tumors). The final section is on interrelationship of viruses and the intra- and extracellular factors in neoplasia. Included is a study of the role of a "transmissible factor" in leukemia induction by radiation + urethan (L. Berenblum); combined action with other carcinogens (M. H. Salaman, et al.); oncogenicity of human adenovirus (J. J. Trentin, Y. Yabe and G. Taylor); lymphoma in mice treated with 4-nitroquinoline N-oxide (R. Kinoshita and T. Tanaka); "newer" and "older" viruses (M. R. Hilleman); a children's cancer dependent on environment (D. Burkitt); and a brief review of the role of viruses in relation to cancer (E. L. Horsfall, Jr.). (Approx. 870 references in the cited chapters)

64-2060 ON THE GEOGRAPHIC DISTRIBUTION OF SKIN CANCER. (E.) Profirov, D. (Dept. Skin Dis., I. P. Pavlov Med. Inst., Plovdiv, Bulgaria). *Folia Med. (Plovdiv)* 5(3):206-210, 1963.

A review of reported data concerning the geographic distribution of skin cancers appeared to confirm that their incidence relative to all dermatoses increased with decreasing latitude, reaching a max. in areas close to the equator. The author's own analysis of 2060 Bulgarian pts. also indicated that more than 80% were individuals whose occupations had exposed them for many yr. to strong sunlight. In 95.9% of the cases, localization was in the exposed areas of the head and face. At the same time, he points out that the role of cutaneous pigmentation also appears to be a predominant one, with peoples who are dark-eyed, with dark skin and hair, contracting the disorder comparatively rarely, even in tropical or subtropical climates. (24 references)

- 64-2061 WHY TWO HUNDRED YEARS OF SCIENTIFIC RESEARCH ON CANCER HAVE BEEN A DISILLUSIONMENT. (Fr.) Voisin, A. Rev. Path. Gen. 63(749):631-672, 1963.

In concluding that nutrition is one of the principal factors in both carcinogenesis and the organism's ability to ward off cancer, the author states that the evolution of civilization has multiplied active carcinogens rapidly while diminishing the organism's mechanisms of defense by introducing white bread, polished rice, refined sugar and purified salt, and replacing water drawn from deep wells with allegedly purified river water. In addition, and even more serious, the widespread use of fertilizers (especially those containing potassium or nitrogen) has modified the mineral content of the soil and its products, creating a magnesium deficiency in grazing animals and a copper deficiency in grains and plants, with eventually resulting deficiencies of both in man (who uses the grains, plants and animals for food) which in turn predispose to cancer. A number of works are cited which show that copper antagonizes the carcinogenic effect of dimethylaminoazobenzene. The author's study of the geographic distribution of cancer cases confirmed a direct relationship between cancer incidence and types of soil; with incidence highest in areas where the soil also induces a copper deficiency in grazing animals. Such soils are deficient in copper either because they are abnormally rich in zinc or are of a heavy, poorly aerated texture, and rich in undecomposed organic matter. See also CRA 1(12):#2112, 1964. (Approx. 33 references)

- 64-2062 INFLUENCE OF AGING ON MALIGNANCY. (E.) Cowdry, E. V. (Scientific Assoc., St. Louis, Mo.). Asian Med. J. 6(10)879-893, 1963.

A general review of the problems encountered in interpreting incidence and mortality statistics includes material reported previously in CRA 1(3):#517, 1963. (13 references)

- 64-2063 MODIFICATIONS OF THE CHROMOSOMES IN THE CELLS OF PATIENTS WITH ACUTE LEUKEMIAS. (Fr.) Ruffié, J. (Blood Transfusion Ctr., Toulouse, France). Nouv. Rev. Franc. Hemat. 3(6):830-844, 1963.

A review of chromosomal abnormalities reportedly occurring in some pts. with acute myeloid or lymphatic leukemias (and in 1 case of acute monoblastic leukemia) is followed by a summary of the theories which have been advanced to account for these changes. The author concludes that it is possible that a severe disturbance of the chromosomes of group 21 (e.g., loss, fractionation, or trisomy) impedes or delays maturation of the leukocyte; while subsequent development of an abnormal clone with supernumerary chromosomes is followed by a series of successive aneuploidies which precipitate the clinically demonstrable stage of the disorder (possibly after having affected a particular pair of the 6-12 group). In discussion, J. Lejeune spoke of the technical difficulties involved in studying such chromosomal changes; and Salmon pointed out the probability of an interaction of several, essentially independent genetic systems, involving both the structure of the antigen and that of the isoagglutinin. Bessis reported indications of the existence of a common precursor for erythrocytes and leukocytes, and evidence that the Philadelphia chromosome had an active influence only in the latter. Ford expressed the belief that chromosomal changes were not a causal factor in the leukemias, but had a profound effect on the progress of both this and other neoplastic disorders. (39 references)

- 64-2064 CURRENT CONCEPTS OF CANCER. (E.) Horsfall, F. L., Jr. (Sloan-Kettering Inst. Cancer Res., New York). Canad. Med. Assn. J. 89(24):1224-1229, 1963.

See CRA 1(9-10):#1661, 1964. (26 references)

- 64-2065 CANCER AND THE ADRENAL. (E.) Huggins, (Ben May Lab., U. Chicago, Ill.). Ann. Roy. Coll. Surg. Eng. 33(6):337-343, 1963.

Review of work on experimental mammary cancer with a discussion of the nature of the tumors evoked, the molecular structures of the carcinogenic aromatics and their relation to carcinogenicity, the action of 9,10-dimethyl-1,2-benzanthracene on the testis and the adrenal gland and, finally, the protection of the adrenal gland by pretreatment with many aromatics. (See also CRA 1(5):#796; ibid., #878; and ibid., 1(6):#1113, 1963.) (19 references)

See also abstract nos.: 2137, 2164, 2167, 2186

PHYSICAL CARCINOGENESIS

64-2066 ON THE QUESTION OF DELAYED INJURY AFTER TREATMENT WITH THORIUM-X. (Ger.) Kutz, G. (Annastift Orthoped. Clin., Hanover, Germany). *Zschr. Orthop.* 97(4):474-482, 1963.

Of 92 pts. treated with Thorium-X for Bechterew's disease during 1952-1961, 1 pt. died of panmyelopathy after 10 inj. of Thorium-X (Th-X). Contrary to reports of others, the authors found atypical cells in the bone marrow, especially nuclear anomalies in immature WBC, as long as 5 yr. after treatment with 200 e.s.U Th-X, 2x/wk. Patients receiving only 1 treatment/wk. (200 e.s.U; total dose 2000-2400 e.s.U) showed such anomalies only in isolated instances.

64-2067 THE RELATIONSHIP BETWEEN RADIATION INJURY TO THE SKIN AND SUBSEQUENT MALIGNANT CHANGE. (E.) Neuman, Z. (Dept. Plast. Maxillofacial Surg., Mayer de Rothschild Hadassah J. Hosp., Jerusalem, Israel), N. Ben-Hur and J. Shulman. *Surg. Gynec. Obstet.* 117(5):559-562, 1963.

Patients (85) suffering from radiodermatitis admitted for plastic repair between 1954-1962 were divided into 2 groups. Among 45 who received radiation for malignant conditions and who survived long enough, basal cell carcinoma developed in 2, with latent periods of 12 and 13 yr. Among 40 originally irradiated for benign conditions, carcinoma developed in 13. In this group latent periods were: 1 case, 5 yr.; 7 cases, 20-28 yr.; 4 cases, 30-32 yr.; 1 case, 36 yr. Patients who had long, so-called "conservative" treatment showed transitional basal-squamous cell, and finally squamous cell, carcinoma.

64-2068 INDUCTION OF PLASMA CELL TUMORS AND SARCOMAS IN MICE BY DIFFUSION CHAMBERS PLACED IN THE PERITONEAL CAVITY. (E.) Merwin, J. M. (NCI, Bethesda) and L. W. Redmon. *J. Nat. Cancer Inst.* 31(4):997-1017, 1963.

Plasma cell tumors are induced in BALB/c mice by empty chambers of 3 materials: Plexiglas, Millipore filter membrane, and an adhesive. Several findings suggest that mechanical trauma or other irritating conditions are important. Thus, the tumor incidence increases as the chamber size and the amount of fibrosis increase. Also, irritating Plexiglas borings induce many tumors, whereas nonirritating rings or fibers induce few tumors. Evidence suggests that factors associated with the presence of tissue within the chambers may increase tumor incidence. In several other strains of mice few or no plasma cell tumors are caused by diffusion chambers and the incidence does not increase with chamber size. Sarcomas, also, are induced by diffusion chambers. In BALB/c and perhaps the SWR strains are

particularly susceptible to sarcoma induction. The presence of tissue inside the chambers seems, under certain conditions, to increase sarcoma incidence. More sarcomas arise on the recessed than on the flat side of the chambers.

64-2069 SPECIAL SENSITIVITY OF NEWBORN MICE TO THE LEUKEMOGENIC ACTION OF X-RAYS. (Fr., Abstract) Rudali, G. (Lab. Genet., Curie Found., Paris). *Int. J. Radiat. Biol.* 6(4):374-375, 1963.

One-third of C57BL mice which were irradiated (125 r x 5) after 40 days of age developed leukemia. When irradiation was initiated at birth, the rate increased to 80%. In hybrid F1(C57BL x AKR) in which the incidence of spontaneous leukemia was low (11% after an av. latency of 600 days), irradiation under the conditions described above brought about many leukemias: 63% after a latency of 200 days if treatment began at 40 days of age and 83% with an av. latency of 166 days when irradiation was begun at birth. No leukemias appeared when newborn C57BL were irradiated with a single dose of 250 r. No leukemias developed in approx. 100 XVII/G mice irradiated at 40 days of age (125 r x 5) during a period of observation of 12-24 mo. Early results indicated that similar results could be expected from animals irradiated at birth. A large number of leukemias were observed in incomplete experiments in which F1(XVII/G x AKR) mice were irradiated at birth although normally these mice showed a low incidence of spontaneous leukemias.

64-2070 INFLUENCE OF WHOLE BODY X-IRRADIATION AND OF THE ADMINISTRATION OF FETAL LIVER ON SPONTANEOUS LEUKEMOGENESIS IN AKR MICE. (Fr., Abstract) Duplan, J. F. (Curie Found., Paris). *Int. J. Radiat. Biol.* 6(4):362, 1963.

The latency and frequency of leukemias were normal in AKR mice following sublethal and 70% lethal (460 r and 600 r, resp.) doses of total body irradiation. When the total body irradiation was followed by admin. of isologous fetal liver, the incidence was not changed but after 600 r the latency was prolonged. In mice which were subjected to 800 r, total body irradiation (100% lethal) followed by an inj. of AKR bone marrow, the incidence of the leukemias was reduced to 21% (75% in controls). A reduction in the frequency of leukemia could also be obtained if homologous (XVII or CH3) fetal hematopoietic cells were inj. following 460 r and especially 600 r.

64-2071 CO-LEUKEMOGENIC ACTION OF CROTON OIL IN THE DEVELOPMENT OF LEUKEMIA BY X-RAY-IRRADIATION. (Jap.) Irino, S. (Dept. Int. Med., Okayama U. Sch. Med., Japan), T. Sezaki,

K. Ikejiri, S. Sota and M. Suzaki. Igaku To Seibutsugaku (Med. Biol.) 67(4):218-223, 1963.

Induction of leukemia (T = thymic, NT = non-thymic) was studied in 30-40-day-old RF mice of both sexes after admin. of X-irradiation and/or croton oil (5% in benzene, on the skin, 2x/wk. for 20 wk.). After an observation period of 1 yr., incidence of leukemia after 450 r, 350 r and 250 r, was, resp.: 9/17 (53%, 4T + 5NT); 41/53 (77%, 20T + 20NT + 1 myeloid); 3/12 (25%, 1T + 2NT). After 150 r no leukemias developed in 8 mice. When irradiation with 350 r and 250 r was followed immediately by application of croton oil, incidence of leukemia was, resp., 9/13 (69.2%) and 6/11 (54.5%). When 250 r and 150 r was followed after 1 wk. by croton oil, incidence of leukemia was, resp., 4/10 (40%) and 4/11 (36.7%). Croton oil alone caused no leukemia in 8 mice. Among controls, lymphatic leukemia occurred spontaneously in 2/300 (0.7%). The authors conclude that in the production of leukemia in mice, X-irradiation acts as the initiating, and croton oil as the promoting agent.

64-2072 TUMORS FROM PLASTIC SUBSTANCES AND THE NEW THEORY ABOUT CANCER. (It.)

Sirtori, C. (Dept. Anat. Path., Inst. Cancer, Milan, Italy). Minerva Med. 54(96):3686-3688, 1963.

Following a review (19 references) of experimental tumor induction by implantation of film, other plastic substances, resins, etc., the author concludes that Virchow's theory of carcinogenesis by nonspecific irritation has increasingly strong biochemical and practical support. He points out that experimental tumors induced as above are very slow in developing, suggesting that the possible carcinogenic effects of the use of contact lenses, dental and other prostheses, et al., may not become evident in man for another 5 yr. or more.

64-2073 LEUKEMIA AND BACKGROUND RADIATION IN NORTHERN NEW ENGLAND. (E.) Segall, A. (Dept. Epidemiol., Harvard U. Sch. Public Health, Boston, Mass.). Blood 23(2):250-261, 1964.

When the radioactivity in bedrock underlying the 1178 minor civil divisions of the States of Maine, New Hampshire, and Vermont were estimated by radio-geological analysis, values were found to range from 5-45 ppm equivalent uranium. When the divisions were grouped into 4 categories according to mean equivalent uranium conc. in underlying bedrock, there was a maximal difference in annual dose-rate of 14.65 mrad/yr. No statistically significant correlation existed between the amount of such background radiation in particular areas

and the incidence of deaths from leukemia in the 30-yr. period of study or within successive decades. The author points out that these findings do not allow rejection of the hypothesis that leukemia mortality varies with background radioactivity if the dose response relationship is of the order of that estimated from studies in human at doses of 100 rads or greater. Adequate testing seems unlikely in the U. S. where background radiation is relatively small.

64-2074 MYELOFIBROSIS WITH MYELOID METAPLASIA IN SURVIVORS OF THE ATOMIC BOMB IN HIROSHIMA.

(E.) Anderson, R. E. (Atomic Bomb Casualty Comm. Hiroshima, Japan), T. Hoshino, and T. Yamamoto. Ann. Intern. Med. 60(1):1-18, 1964.

During a 10-year period of observation, on the basis of autopsy findings in 10 pts. with generalized idiopathic myelofibrosis with myeloid metaplasia exposed to the atom bomb blast in 1945 in Hiroshima, the incidence has been shown to be inversely proportional to the distance from the hypocenter, with the highest rate among those most proximally exposed. This incidence has proved to be 4.5x greater than among the non-exposed autopsy population seen by the Atomic Bomb Casualty Commission and 18x greater than the autopsy incidence in Japan as a whole. (The authors point out that the arbitrary demarcation point for "non-exposure" was initially accepted as 10,000 meters from the hypocenter, and has proved to be unduly conservative.)

64-2075 MITOTIC EFFECTS OF IONIZING IRRADIATION ON MALIGNANT AND BENIGN EPIDERMAL HYPERPLASIA IN THE MOUSE. V. EFFECTS OF SINGLE DOSE CONTACT IRRADIATION AFTER 10 DAYS' PRETREATMENT WITH A CARCINOGEN OR A TUMOR ENHANCING AGENT.

(Ger.) Setälä, K. (Inst. Pathol. Anat., U. Helsinki, Finland), B. Lindroos and O. Nyyssönen. Strahlentherapie 122(4):565-590, 1963.

A continuation of the studies reported in CRA 1(2) #146 and #200, 1963, with the total of mitotic figures analyzed increased to 102,500 and that of non-dividing nuclei to 1,703,277. In female RA mice exposed to a single, contact dose of radiation from $Sr^{90} + Y^{90}$ (1000 rad/9 min.), malignant epidermal hyperplastic tissue induced by pretreatment with 9,10-dimethyl-1,2-benzanthracene (which showed a significantly lower mitotic rate but abnormal cell maturation) was significantly more susceptible than benign epidermal hyperplastic tissue induced by pretreatment with Tween 60 (which had a significantly higher mitotic rate in the presence of normal or nearly normal cell maturation). No single type of mitotic disturbance was specific for the irradiation response in either epidermal condition.

See also abstract nos.: 2044, 2055, 2081, 2134

CHEMICAL CARCINOGENESIS

64-2076 EFFECT OF DIFFERENT DOSES OF METHYLTHIOURACIL, THYROIDIN AND HEXAMETHONIUM ON CARCINOGENESIS. (Rus., Abstract) Skatkov, M. E. Vop. Onkol. 9(9):118-119, 1963.

Tumors in the rat induced by 0.5 mg DMBA were stimulated in their growth by inj. of 10, 20, and 40 mg/day of methylthiouracil (M), thyroidin (T), and hexamethonium (H). However, M at a dose of 10 mg/day and T at a dose of 100 mg/day inhibited the carcinogenic process. T at 50 mg and H at 40 mg did not influence carcinogenesis. The anticarcinogenic effect of M, T, and H is due to the disruption of the oxidative processes of the cell; however, the inhibition of the carcinogenic process by large doses of M and T is nonspecific and apparently connected not only with their injurious effect on the cells and tissues of the organism, but also to marked interference with compensatory adaptive reactions and proliferative processes.

64-2077 CONSTITUTIONAL AND HEREDITARY ASPECTS OF ENDOMETRIAL CARCINOMA. (Ger.) Sanders-van Halewijn, E. A. (Gynec. Clin., U. Utrecht, The Netherlands), F. de Waard, J. L. van der Boon, E. Tonkes and L. Meinsma. Zschr. Geburtsh. Gynaek. 161(1):77-93, 1963.

From a statistical study of 272 pts. with carcinoma of the corpus uteri and of 565 women controls, the previously observed concurrence of carcinoma of the corpus uteri with obesity, hypertension, disturbed glucose tolerance, and late menopause was confirmed. Cytologic studies (by others) have shown that there occurs in these women a continued, extra-ovarian, adrenal production of estrogen. Hence the authors assume, that at the lateness of onset of the menopause is related to a time during which the diminished estrogen formation by the ovaries is replenished by an extra-ovarian production of estrogen by the adrenals; this leads to anovulatory menstrual bleeding which continues for some time. Since there are statistical indications that such adrenal estrogen production has a heritable basis, this suggests that there is a heritable predisposition to carcinoma of the uterine body.

64-2078 SOME BIOLOGICAL CHARACTERISTICS OF LIVER CELLS IN THE COURSE OF EXPERIMENTAL CARCINOGENESIS IN MICE. (E.) Gel'shtein, I. (Inst. Exptl. Oncol., Acad. Med. Sci. USSR, Moscow). Acta Un. Int. Cancr. 19(3-4): 39-51, 1963.

Further comment is presented of the work abstracted in CRA 1(4):#655, 1963. Mice received 20 skin injections with o-aminoazotoluene (OAAT; 1% in benzene) over a period of 7 wk. Hepatectomy was performed at intervals from 1-360 days after the

end of carcinogenic treatment; animals were killed 48 hr. after operation. Up to 18 wk. after the start of the experiment mitosis was inhibited (av. mitotic coefficient (Mc) in treated mice was 2.5, controls 43.1). From the third month, focal adenomatous nodules began to appear and at this time the reaction to partial hepatectomy was also focal: Mc was high (30.5) among cells of the nodules and low in surrounding dystrophic areas (2.3). In control livers mitoses were distributed at random (Mc 30.6). In established tumors OAAT no longer inhibited the mitoses; after partial hepatectomy these cells showed a slight increase in mitotic rate which was independent of previous treatment. Organ specific antigens from normal mouse liver were compared with those from liver at various stages of carcinogenesis induced by OAAT and CCl₄. Only 3 of the 5 known organ-specific antigens of normal liver were found in anti-precancerous sera.

64-2079 THE REACTION OF NORMAL AND TUMOR CELLS TO FACTORS CAPABLE OF DEPRESSING OR STIMULATING PROLIFERATION. (Rus.) Vasil'ev, Iu. M. and V. I. Gel'shtein. Vop. Onkol. 9(5): 61-67, 1963.

In normal mice, CCl₄ (0.04 ml) caused multiple necrosis of the central hepatic lobules; no such changes were evident in mice with CCl₄-induced hepatomas or OAAT-induced Hepatomas 37 and 46. After partial hepatectomy 48 hr. previously, the mitotic coefficient was increased in mice with Hepatoma 46, in intact mice or in those painted before surgery with a 1% soln. of OAAT in benzene for 1 wk. or 1 mo. Low conc. of DMBA depressed the growth of normal rat connective tissue; however, growth of primary cultures of DMBA-induced sarcoma was inhibited only with high conc. Sarcoma 45 (a rat transplantable tumor originally induced by DMBA) was highly resistant to DMBA. Similar results were obtained with benzpyrene and methylcholanthrene. Sarcocystin (0.001-0.1 mg/ml) did not affect the growth of normal tissues, but decreased the growth of tumor cells. A review is also presented of other published work on the behavior of normal and tumor tissues treated with DMBA, scarlet red, and the use of "combined transplants" (small amount of tumor cells and large amount of lethally damaged tumor, or normal cells of embryos or mature animals). A cell-free filtrate of Ehrlich ascites carcinoma admin. i.p. a few min. before the inoc. of Ehrlich tumor markedly increased tumor take and accelerated the growth of tumor cells; no stimulation of growth was noted when the filtrate was admin. s.c. and tumor cells i.p. Isologous serum of normal mouse had no stimulating effect. Following presentation of the paper there was a discussion of the sensitivity of tumor cells to carcinogens, irradiation, hepatectomy, normal cell suspensions and other factors.

- 64-2080 INDUCTION OF FIBROSARCOMA IN THE PRIMATE TAMARINUS NIGRICOLLIS. (E.) Levy, B. M. (Dent. Branch, U. Texas, Houston). Nature (London) 200:182-183, 1963.

Injection of 20-methylcholanthrene (correction for 2-methylcholanthrene; 2 mg s.c. in olive oil) into 5 marmosets (Tamarinus nigricollis) produced no change at the site of inj. in 3 animals that died 1 mo. later of upper respiratory infection, nor in 1 survivor. However, one animal that died after 10 mo. of an upper respiratory infection showed dermal changes similar to those of seborrheic keratosis at the inj. site, and an underlying non-metastasizing tumor resembling a fibrosarcoma.

- 64-2081 CHANGES IN CELL-NUCLEI, PARTICULARLY OF THE EPITHELIUM, AFTER CARCINOGENIC ACTION. (Ger.) Zuhelle, E. (Blondelstr. 11, 51, Aachen, Germany). Z. Aerztl. Fortbild. 52(2):135-137, 1963.

A discussion of the mechanism of carcinogenesis in which the author reviews his earlier work on the action of radium radiation on rabbit skin and of s.c. inj. of Fowler's soln. on nuclear changes in the cells of the wattles and connective tissue of the rooster and attempts to reconcile Bauer's mutation theory with the fermentation theory of Warburg by suggesting that carcinogens first affected nuclear damage which, in turn, affected cell respiration.

- 64-2082 PROGESTERONE AND TUMOUR METASTASIS. (E.) Poel, W. E. (Grad. Sch. Public Health, U. Pittsburgh, Pa.) and N. Haran-Ghera. Lancet 2:970-972, 1963.

A more detailed account of the paper abstracted as CRA 1(6):#1063, 1963.

- 64-2083 CARCINOMA OF THE SCROTUM, FOLLOWING LONG-TERM, UNSUPERVISED TREATMENT OF AN ECZEMA WITH A TAR DERIVATIVE. (Ger.) Sonneck, H. J. (Dermatol. Clin., Martin-Luther U., Halle-Wittenberg, Germany) and H. Koch. Derm. Wschr. 148(40):352-355, 1963.

Following 8 yr. of unsupervised treatment of an eczema of the scrotum with a coal tar derivative (no details), a 63-year-old man underwent surgery for a cutaneous, scrotal, precancerous papilloma but continued self-medication of the eczema, as before. Five yr. later he underwent orchiectomy for a basal cell carcinoma of the scrotum.

- 64-2084 REACTION OF THE CARCINOGEN DIMETHYL-NITROSAMINE WITH NUCLEIC ACIDS IN VIVO. (E.) Craddock, V. M. (Med. Res. Coun. Lab., Carshalton, Surrey, England) and P. N. Magee. Biochem. J. 89(1):32-37, 1963.

After i.p. inj. into female Porton strain Wistar rats of C^{14} -dimethylnitrosamine (C^{14} -D; 10 mg (10 μ C)/kg), methylation of liver RNA and kidney RNA reached a max. in 5-12 hr. and then decreased, reaching a very low level at 3 wk. In the liver, where methylation was most extensive, there was a rapid initial loss of the RNA methyl group during the first 2 days which was not dependant on concomitant necrosis. After inj. of 30 μ C C^{14} -D, liver DNA and kidney DNA became rapidly methylated, with a much higher peak for liver DNA; loss of the methyl group occurred more rapidly from liver, more slowly from kidney. Rapid incorporation of normal C_1 metabolic-pool intermediates took place into RNA and DNA of liver and kidney; incorporation with liver DNA continued after the first 24 hr. because of tissue regeneration.

- 64-2085 EXPERIMENTAL AND CLINICAL STUDIES ON THE FLUOROBIOLOGY OF THE CERVIX. II. NUCLEIC ACIDS' VARIATIONS IN EARLY STAGES OF INDUCED CARCINOGENESIS. (E.) Sherif, M. (U. Alexandria, Egypt). Acta Obstet. Gynec. Scand. 42(2):192-199, 1963.

Cervical smears of C3H mice were collected every 24 hr. x 4 after a single application to the cervix of 20-methylcholanthrene (MC; 1% in acetone). Vital staining was accomplished with acridine orange (10 mg/kg i.p. 3 hr. before smears were obtained). Fluorescent MC crystals were most brilliantly seen at 24 hr. and in the cytoplasm of squamous cells; there was no trace of crystals in the nuclei at any time. At 48 hr. the previously faintly outlined nuclei of a large number of cells showed marked increase in intensity of the fluorescence, especially at the center. Many cells showed yellow-golden fluorescence of the cytoplasm starting at the outer border of the cell, at one or more points. While generally the spectral emission for the smear was in the green range, some cells showed polychromasia. At 72 hr. the nuclei showed intense fluorescence, both at the center and at the periphery, with evident shift of the color towards orange. Most cells showed yellow-golden cytoplasmic fluorescence of high intensity. At 96 hr. MC crystals were no longer identifiable and the nuclear and cytoplasmic changes became more pronounced. It is concluded that in induced cervical carcinogenesis MC interacts with the cytoplasm, conceivably with the protein moiety of cytoplasmic ribonucleate, with consequent qualitative molecular change in cytoplasmic RNA. Intranuclear nucleic acids show quantitative increase induced by the carcinogen but not due to direct interaction with it.

- 64-2086 HISTOCHEMICAL STUDIES OF THE ACTIVITY OF A NON-SPECIFIC ESTERASE IN TRANSPLANTABLE TUMORS. (Ger.) Butschak, G. (Inst. Exptl. Cancer Res., German Acad. Sci., Berlin). Acta Biol. Med. German. 11(3): 417-423, 1963.

In the livers of rats bearing transplanted Hepatoma I or N2, or hepatoma induced by diethylnitrosamine, α -naphthylacetate esterase activity was approx. 3/5 as great as that seen in normal rat livers, although no significant difference could be demonstrated in the corresponding cutaneous tissues. In the remaining tumors tested, there were no marked differences from normal tissues; enzyme activity values were lower than those of normal hamster, and normal as well as newborn rat and mouse liver. These tumors were: (in mice) Ehrlich carcinoma, DMBA-carcinoma, DMBA-carcinoma 450, Sarcoma 37, Sarcoma Sala, DMBA-sarcoma and methylcholanthrene-induced sarcomas; (in rats) Walker carcinoma, Yoshida, Jensen, or R312(BB/T2) sarcoma; (in hamsters) benzo(a)pyrene-induced sarcoma or BB/T2 sarcomas.

64-2087 HOST FACTORS INFLUENCING THE BEHAVIOR OF SUBCUTANEOUS SARCOMAS INDUCED BY 3,4,9,10-DIBENZOPYRENE IN C57BL/6 MICE. (E.) Homburger, F. (Bio-Res. Inst., Cambridge, Mass.), A. Treger and J. R. Baker. Cancer Res. 23(9):1539-1544, 1963.

In male and female C57BL/6 Jax mice inj. s.c. with 3,4,9,10-dibenzopyrene (500 μ g, in peanut oil), caloric restriction severe enough to prevent significant wt. gains during the period of induction of sarcomas significantly prolonged latent times. Rate of tumor formation was lower in females than in males, but was independent of body wt. at time of carcinogen inj., subsequent growth rate, and (in males only) of the age at the time of inj.

64-2088 CADMIUM-INDUCED INTERSTITIAL CELL TUMORS IN RATS AND MICE AND THEIR PREVENTION BY ZINC. (E.) Gunn, S. A. (Dept. Path., U. Miami Sch. Med., Coral Gables, Fla.), T. C. Gould and W. A. D. Anderson. J. Nat. Cancer Inst. 31(4):745-759, 1963.

A single s.c. inj. of cadmium chloride (Cd) to rats and mice selectively damaged the vascular supply of the testis and resulted in complete necrosis of the seminiferous tubules and interstitial tissue. After a few wk. interstitial tissue regenerated, and approx. 1 yr. later 70-80% of the animals showed evidence of interstitial cell tumor (ICT) formation. The induction of ICT by Cd was prevented by the simultaneous admin. of a physicochemically similar element, zinc. Studies on the hormonal status of rats treated with Cd 3 mo. previously indicated that the content of interstitial cell-stimulating hormone (ICSH) of pituitary glands was higher than control levels. Normal-appearing, regenerating Leydig's cells were not functioning normally, however, as indicated by lowered accessory-gland size and function. This was further emphasized by hormonal studies that showed the cadmium-treated rats were completely unresponsive to admin. ICSH.

64-2089 FLUORESCENT SPECTRUM INVESTIGATION OF THE PRODUCTS OF SMOKING TOBACCO GOODS. (E.) Dikun, P. P. and S. G. Chuskin. Translation of Voprosy Onkologii (USSR) 1959, v. 5(7), pp. 34-38. Cited in Tech. Transl. 10(9):1015, 1963.

Fluorescent spectroscopy of the smoke of 3 brands of cigarettes (employing a smoking machine) revealed the presence of 3,4-benzopyrene. Full translation available from the Office of Technical Services, number 63-18462, at a cost of \$1.10.

64-2090 ON THE CANCEROGENIC ACTIVITY OF TOBACCO TARS. (E.) Gritsyute, L. A. and A. I. Mironova. Translation of Voprosy Onkologii (USSR) 1960, v. 6(8), pp. 25-33. Cited in Tech. Transl. 10(9):1016, 1963.

After topical application of tobacco combustion products, tumors of the skin developed in 8/238 mice; sarcoma of the s.c. tissue at the place of introduction in 1/82 rats; multiple papilloma in 2/8 rabbits. The small carcinogenic effect obtained indicate these changes are pretumoral and correspond to the physical analysis of the tobacco tar according to which the amount of 3,4-benzopyrene was very small. Full translation available from Office of Technical Services, number 63-16659, at a cost of \$1.60.

64-2091 EXPERIMENTAL STUDIES ON THE INFLUENCE OF RETICULO-ENDOTHELIAL SYSTEM UPON THE INDUCTION OF MALIGNANT GASTRIC NEOPLASMS. (E.) Ojima, Y. (2nd Surg. Div., Kyoto U. Sch. Med., Japan). Arch. Jap. Chir. 32(4):451-477, 1963.

After inj. into the pyloric or fundic portion of the glandular stomach of 4-5-month-old Wistar rats of 20-methylcholanthrene (MC; 0.4 or 0.8 mg suspended in methocel or emulsified in olive oil), animals were sacrificed at various intervals up to 607 days. Among 319 intact rats, there were 3 with adenocarcinoma and 8 with sarcoma; 50 showed cancer-like, invasive lesions. Precancerous changes were noted in 193: 183 adenomatous proliferation and 10 intestinal metaplasia. In contrast, among 85 rats subjected to splenectomy at the time of MC inj., there were 2 with adenocarcinoma, 12 with sarcoma; 25 showed cancer-like invasive lesions. Precancerous changes were seen in 70: 65 adenomatous proliferation and 5 intestinal metaplasia. Metastases were more frequent among splenectomized rats. The apparent potentiation of the carcinogenic action of MC by splenectomy seemed ascribable to decrease in general resistance of the rats. There was no marked difference relative to the use of methocel or olive oil. Malignant and precancerous changes were seen more often in the pyloric than in the fundic portion of the stomach.

- 64-2092 INDUCTION OF TUMORS BY MEANS OF CHEMICAL CARCINOGENS IN THE HAMSTER. II. A STUDY OF METHYLCHOLANTHRENE, BENZPYRENE AND DIMETHYLBENZANTHRACENE INJECTED IN VARYING DOSES. (Fr.) Rivi re, M.-R. (Lab. Exptl. Med., Cancer Sci. Res. Inst., Villejuif, Seine, France), I. Chouroulinkov and M. Gu rin. Bull. Assn. Franc. Cancer 50(2):275-289, 1963.

After single s.c. doses of methylcholanthrene (MC), benzpyrene (BP), and 9,10-dimethyl-1,2-benzanthracene (DMBA) to golden hamsters aged 3-6 mo., incidence of sarcomas, was, resp.: 0.005 mg--0/12, 0/12 and 0/12; 0.01 mg--1/12, 1/12 and 4/12; 0.1 mg--9/12, 5/11 and 10/12; 1.0 mg--12/12, 10/12 and 11/12; 10 mg--10/12, 12/12 and 3/3; 20 mg--10/12, 11/12 and no survivors. For MC and BP after 40 mg, incidence of sarcoma was 11/12 and 12/12, resp.; after 60 and 80 mg, incidence was 100% in groups of 8 and 12, resp. The frequency of metastases was also dose-related. The incidence of pulmonary and lymph node metastases, resp., at 1 mg was: MC--10/12, 2/12; BP--6/12, 1/12; DMBA--5/12, 2/12. At 10 mg, it was: MC--7/12, 2/12; BP--8/12, 2/12; DMBA--1/3, 0/3. At 20 mg, it was: MC--10/12, 3/12; BP--8/12, 2/12. In the light of similar studies with mice and rats, the authors conclude that the hamster is the experimental animal of choice for the study of metastatic processes secondary to chemically-induced tumors.

- 64-2093 IN VITRO ACTION OF METHYLCHOLANTHRENE ON THE TESTICLE. (Fr.) Furtado Dias, M. T. (Portuguese Inst. Oncol., Lisbon). Arg. Pat. 35(2):163-169, 1963.

When fragments of testicles obtained from 2-4-day-old mice were incub. for 1 wk. in plasma clot cultures + methylcholanthrene (MC; 10 μ g/ml chick plasma + equal volumes rat plasma and horse serum, and mixed 1:1 with embryo extract) and then removed to MC-free media for 21 days, the only surviving cell types were germinative elements resembling those found in tumors of rats treated with MC, and a few multinucleated giant cells. The cells did not resemble those found in spontaneous testicular tumors in strain H mice. The treated cultures contained numerous mitotic figures, but no mitotic abnormalities. Inoculation of MC-treated cultures into young mice failed to cause tumors, and other studies varying temperature and hormonal environment also failed to clarify the nature or etiology of the spontaneous interstitial cell tumors observed in the H mice.

- 64-2094 EFFECTS OF CORTISONE ON CHEMICAL CARCINOGENESIS IN HAMSTER POUCH AND SUBMANDIBULAR SALIVARY GLAND. (E.) Sabes, W. R. (U. Detroit Sch. Dent., Mich.), A. P. Chaudhry and R. J. Gorlin. J. Dent. Res. 42(5):1118-1130, 1963.

After 2 wk. of standardization (maintenance in a room lighted from 6 A.M. to 6 P.M., then kept dark), the cheek pouches of 6-week-old hamsters were painted with 0.25 μ g of 9,10-dimethyl-1,2-benzanthracene (DMBA) in liquid petrolatum (group I; 9 hamsters); in group II (7 animals), the pouch was painted with cortisone immediately after the carcinogen dried while in group III (13 animals) cortisone was applied prior to the DMBA. While there was no significant difference in latent periods, that of group III was shortest. Incidence of fibrosarcoma (tumors per animal) was, resp., 1.0, 1.57 and 3.08 for groups I, II and III. Microscopically positive findings (pre-invasive and grades 1 and 2 squamous cell carcinoma) occurred in 44.4, 57.1 and 92.3%, resp. The right submandibular salivary glands of groups of 13-17 hamsters were inj. with cortisone followed by DMBA (treated group, I) or with vehicle + DMBA (II), saline + DMBA (III), or DMBA only (IV). Of the half that were treated in the morning (9 A.M. to 12 noon) none of group I had tumors compared to 40.9% in pooled animals of groups II-IV. No such intergroup difference was found among those treated in the afternoon (2-5 P.M.); incidence of sarcoma was, resp., 3/7, 3/7, 4/7 and 1/6. A review of the effect of cortisone on chemical carcinogenesis is also presented (35 references).

- 64-2095 THIN-LAYER CHROMATOGRAPHIC SEPARATION OF BENZO[a]PYRENE AND BENZO[k]FLUORANTHENE FROM AIRBORNE PARTICULATES. (E.) Sawicki, E. (Robert A. Taft Sanitary Engin. Ctr., Cincinnati, Ohio), T. R. Stanley, J. D. Pfaff, and W. C. Elbert. Chem. Anal. 53(1):6-8, 1964.

A description is given for the use of thin-layer chromatography in the identification of polynuclear aromatic hydrocarbons in benzene soluble fractions of airborne particulates. The technic is especially useful, using a cellulose acetate absorbent and ethanol-toluene-water as the solvent to separate 3,4-benzpyrene from benzo(k)fluoranthene (which has an intense band near that of the former) and from members of the "benzpyrene" fraction.

- 64-2096 INHIBITION OF TUMORIGENIC ACTION OF URETHANE BY BUTYL CARBAMATE. (E.) Garcia, H. (Dept. Oncol., U. Chile, Santiago). Biologica (Santiago) (34):11-13, 1963.

In mice (Swiss albino), admin. of ethyl carbamate (urethan; total dose 10 μ moles/g i.p.) followed by painting of the skin with croton oil (0.5% in acetone) induced a total of 26 tumors in 13/30 animals after 40 days; this was reduced by the simultaneous inj. of butyl carbamate (BC; 10 μ moles/g i.p.) to 21 tumors in 7/30. After increase of BC to 50 μ moles/g, incidence was decreased to 3/23 animals (3 tumors). After receiving BC alone (10 μ moles/g) 5/30 animals showed 9 tumors; after 50 μ moles/g, incidence

was 2/28 (4 tumors). Among animals painted with croton oil alone, 1/29 showed a single skin tumor. The only carcinomas found were in the first three groups (one animal in each group).

64-2097 EXPERIMENTAL STUDIES WITH TOBACCO CARCINOGENS AND BLADDER MUCOSA. (E.) Cobb, B. (Div. Urol., U. Washington Sch. Med., Seattle) and J. S. Ansell. Surg. Forum 14: 498-500, 1963.

B/Albino C mice received s.c. a transplant of the bladder of littermate mice in which had been inj. either a concentrate of an acetone extract of urine obtained from heavy smokers with bladder cancer, a nonsmoking pt. with bladder cancer, a nonsmoking pt. without bladder cancer, or with tobacco tar obtained from a "smoking machine" or with the mineral oil vehicle used to suspend all the other samples. After 1 yr. there was marked circumferential perivesical inflammation and in some there was hyperplasia of the mucosa in the cases where the bladder pouches were prepared from the urines of heavy smokers or with tobacco tars. There was slight pleomorphism in those with the greatest amount of hyperplasia. No frank neoplasms were produced. A new implantation of hyperplastic samples in another littermate for an additional 3 mo. produced hyperplasia similar to that of the first sample. In the case of controls (mineral oil and nonsmoking pts.) the mucosa appeared normal.

4-2098 MECHANISMS OF DRUG-INDUCED CARCINOGENESIS. (E., Abstract) Magee, P. N. Biochem. Pharmacol. 112(Suppl.):199-200, 1963.

It is mentioned that nitrosoamines probably are converted into alkylating agents present at the site of the target organ and that these alkylating agents (possibly diazoalkanes) might be carcinogenic by producing modifications of cellular components such as DNA, RNA or cell protein. The author compares this neoplastic transformation to genetic mutation and suggests that the present evidence indicates that if such chemical alteration of nucleic acid is relevant to the induction of cancer the alteration may be quantitatively minute as is thought to be the case in genetic mutation.

4-2099 EFFECT OF ADMINISTRATION OF 4-DIMETHYLAMINOAZOBENZENE (DAB) AND OF 2-ACETYLNAPHTHYLENE (AAF) ON HEPATIC RIBONUCLEASE IN THE RAT. (It.) Calderera, C. M. (Inst. Biol. Chem. U. Torino, Italy), R. Budini and A. Rabbi. Boll. Soc. Ital. Biol. Sper. 38(24):1767-1769, 1962.

Male albino rats (90 days old, weighing 150-200 g), addition of 0.06% DAB to the basic Popper diet had little effect on RNase activity of liver after 7 days but caused about 25% increase in 21

days; 0.04% AAF increased this activity about 30% in 7 days and 50% in 21 days.

64-2100 RELATIONSHIP BETWEEN CARCINOGENIC POWER AND ELECTRONIC TRANSITION ENERGY. (Fr.) Shou-Sin Sung. C.R. Acad. Sci. (Paris) 257(6): 1425-1427, 1963.

A survey of reference texts revealed 172 compounds for which data was available on absorption spectra and carcinogenic activity. No proven carcinogen could be detected in 73 compounds with absorption spectra below 354.5 m μ , whereas 42% of compounds with absorption spectra above 354.5 m μ (neglecting absorption where the logarithm of the extinction coefficient is less than 1.0) were carcinogens, all with absorption peaks between 354.5 and 368.0 m μ . Included in the latter group are 3,4-benzopyrene, 3,4,8,9-dibenzopyrene, cholanthrene, 20-methylcholanthrene and groups of methylbenzanthracenes and methylbenzacridines. The sample surveys appear to be representative of carcinogenic compounds, since it contains 24% carcinogens, about the same number found in previously published series of screened compounds. These results are thought to be in agreement with previous work by the author, demonstrating that for 28 methylbenzacridines, 13/14 carcinogenic compounds have ΔE_2 below 1163, and 11/14 noncarcinogenic compounds have ΔE_2 above this value.

64-2101 STUDIES ON THE ETIOLOGY OF BOVINE BLADDER CANCER. (E.) Bryan, G. T. (Dept. Surg., U. Wisconsin Sch. Med., Madison), R. R. Brown and J. M. Price. Ann. N.Y. Acad. Sci. 108(Art. 3):924-937, 1963.

Presented are the times required for elution of 50% of each of 16 suspected carcinogens individually compressed in cholesterol pellets which were implanted into the bladders of female Swiss mice. The times varied between 0.7 days for the 8-methyl-ether of xanthurenic acid to 107 days for N-hydroxy-2-acetylaminofluorene. Under these conditions, N-hydroxy-2-acetylaminofluorene, 2-naphthylhydroxylamine, N-acetyl-2-naphthylhydroxylamine, 3-hydroxy-1-kynurenine, 3-hydroxyanthranilic acid, xanthurenic acid and 8-hydroxyquinoladic acid were found to produce more bladder tumors than were found in controls implanted with pellets containing only cholesterol. In a preliminary study, 2-naphthylhydroxylamine in 52 treated animals led to the highest proportion of invasive carcinomas (13/15).

64-2102 EFFECT OF NEUROSIS ON APPEARANCE AND DEVELOPMENT OF INDUCED MAMMARY GLAND TUMORS IN RATS. (E.) Lo Sing-Mao (Bogomolets Inst. Physiol., Kiev, Uk. SSR). Fed. Proc. (Suppl.) 22(6):1241-1244, 1963.

See CRA 1(4):#645, 1963.

64-2103 EXPERIMENTAL PRODUCTION OF PRECANCER AND CANCER OF THE STOMACH. (E.)

Solov'ev, A. A. (Inst. Normal Path. Physiol., Acad. Med. Sci. USSR, Moscow), E. D. Klimenko, N. A. Nilova and O. M. Pozdnyakov. Fed. Proc. (Suppl.) 22(6):1245-1247, 1963.

See CRA 1(1):#85, 1963.

64-2104 CARCINOGENESIS TESTS OF TWO INORGANIC ARSENICALS. (E.)

Baroni, C. (Inst. Anat., U. Pavia, Italy), G. J. van Esch and U. Saffiotti. Arch. Environ. Health (Chicago) 7(6):668-674, 1963.

In one group of 5-9-week-old Swiss mice, arsenic trioxide was admin. p.o. as a 0.01% soln. in drinking water; in another, this treatment was supplemented by topical application of a 0.3% (wt./vol.) croton oil soln. to the skin, 2x/wk., beginning 2-4 days after initiating treatment; and in a 3rd group, a single dose of 9,10-dimethyl-1,2-benzanthracene (DMBA) in 1% mineral oil was applied to the skin 7 days before initiating treatment. A 4th group, 7 days before treatment with the As₂O₃, received urethan by gastric intubation, 30 mg in 0.2 ml water, repeated after 3 days; and a 5th received the same pretreatment + applications of croton oil during the treatment period. All tests failed to demonstrate any carcinogenic, initiating, or potentiating activity of As₂O₃. No carcinogenic, initiating, or potentiating activity was shown in 4 groups of mice treated with skin applications of sodium arsenate (approx. 0.06 ml of soln. containing 15.8 g/l in a 2.5% Tween 60 soln. 2x/wk.): A. the agent alone; B. + croton oil during treatment period; C. agent alone prepared with Tween 80 instead of Tween 60 and with pretreatment with DMBA; D. agent in Tween 80 and with pretreatment with urethan. In view of available evidence indicating that exposure to arsenic is a hazard in humans, the authors urge further study of its role in carcinogenesis.

64-2105 ADENOCARCINOMA IN THE LUNGS OF MICE EXPOSED TO VAPORS OF 3-NITRO-3-HEXENE. (E.)

Deichmann, W. B. Biochem. Pharmacol. 12(Suppl.):159, 1963.

See CRA 1(7):#1238, 1963.

64-2106 DISCUSSION OF THE NATURE OF RENAL TUMORS INDUCED IN RATS BY DIMETHYLNITROSAMINE. (Fr.)

Riopelle, J.-L. (Dept. Pathol. Anat., U. Montreal, Canada) and G. Jasmin. Rev. Canad. Biol. 22(3-4):365-373, 1963.

In prepubescent Sprague-Dawley rats receiving dimethylnitrosamine in sesame oil (0.5 mg 2x/day x 6 p.o.), renal tumors were induced in all survivors, with a latency period of 6-7 mo. The mortality was 30%. A dose of 1 mg/day x 6 caused

renal tumors in 100% of survivors by the 7th mo., with a 60% mortality; 0.4 mg 2x/day x 10 caused tumors in 50% of the survivors with a 60% mortality; 0.3 mg 2x/day x 6, in 50%, with a 40% mortality; 0.2 mg 2x/day for 1 mo. caused no tumors but the mortality was 20%. One group of tumors, which were well differentiated, was classified as epithelial adenomas arising from the tubules; a second, which was poorly differentiated, as actively proliferating nephroblastomas which tended to resemble anaplastic sarcomas when examined only grossly. The fact that both types of tumor coexisted in the same kidney suggested the further possibility of formation of a third, complex tumor (analogous to human renal carcinosarcoma), by fusion or "collision".

64-2107 QUANTITATIVE ANALYSIS OF THE CARCINOGENIC EFFECT OF DIETHYLNITROSAMINE. (Ger.)

Druckrey, H. (Dept. Surg., U. Freiburg in Breisgau, Germany), A. Schildbach, D. Schmähl, R. Preussmann and S. Ivankovic. Arzneimittelforschung 13(10):841-851, 1963.

In inbred BD II albino rats, diethylnitrosamine, (0.075-14.2 mg/kg/day), admin. in drinking water, exerted a carcinogenic effect (chiefly, in the liver and esophagus) which was independent of total dosage. The total dose effective in 50% of the animals decreased significantly and steadily when lower daily doses were admin. over a correspondingly extended period of time; and the carcinogenic effects of individual doses were shown to be both irreversible and cumulative, although no threshold dose could be established. The mean latency period was consistently inversely proportional (68-840 days) to the amount of total dosage (14.2-0.075 mg/kg/day).

64-2108 INDUCTION OF CANCER BY A SINGLE DOSE OF METHYLNITROSO-CARBAMIDE AND VARIOUS DIALKYL-NITROSAMINES. (Ger., Abstract)

Druckrey, H. (Dept. Surg., U. Freiburg in Breisgau, Germany), D. Steinhoff, R. Preussmann and S. Ivankovic. Naturwissenschaften 50(24):735-736, 1963.

N-Methyl-N-nitrosocarbamide (70-100 mg/kg x 1 i.v.) caused death with tumors of 16/16 BD rats; 5/16 had multiple tumors. Ten animals developed papillomas and 4 carcinomas of the forestomach; other tumors included 8 sarcomas (7 renal, 1 cerebral), 1 plasmacytoma, and 8 carcinomas (3 of the tongue and jaw, 1 mammary and 4 intestinal). Mean latency time was 320 ± 40 days. See also CRA 1(2):#217 and ibid. (7):#1264, 1963.

64-2109 EFFECT OF DEHYDROACETIC ACID ON THE CARCINOGENIC PROCESS IN RAT LIVER DUE TO DIMETHYLAMINO-AZOBENZENE. (Jap.)

Miyaki, K. (Inst. Food Microbiol., Chiba U., Japan), Y. Kagay and R. Nishizawa. Ann. Rep. Inst. Food Microbiol. Chiba U. 15:54-60, 1963.

Groups of Buffalo strain rats (100-120 g at start of experiment) were fed in their basic diet varying amounts of dimethylaminoazobenzene (DAB) and/or the sodium salt of dehydroacetic acid (DHA) for periods varying from 92-152 days. In rats fed only DAB, a total dose of 500 mg or more led to cirrhosis in 100%; histological changes suggestive of cancer were seen in those that received over 800 mg. Rats fed DHA only in a total dose of 1830 mg for 94 days showed no gross abnormalities of the liver but histological examination disclosed atrophic degeneration. Continuous admin. of DHA to rats receiving DAB lowered the incidence of cirrhosis compared to controls that received DAB only. When rats were fed the 2 compounds alternately over a period of 152 days (total DAB, 501-843 mg; DHA, 1100-1530 mg), there was no reduction in cirrhosis and some hepatoma occurred. The effect of DHA on the malignancy of DAB-induced cirrhosis awaits further study.

64-2110 EXPERIMENTAL CANCER AND CIRRHOSIS INDUCED IN THE RAT BY CCl₄. (It.) Costa, A. (Inst. Pathol. Anat., U. Florence, Italy), G. Weber, F. Bartolini St. Omer and S. Campana. Arch. De Vecchi Anat. Patol. 39(1): 303-356, 1963.

When albino rats were subjected to CCl₄ by inhalation over a period of 7 mo. and then observed for a further period of 2-10 mo., 10/30 animals developed multiple hepatomas which could be classified as adenocarcinomas, trabecular carcinoma and dysplastic carcinoma. The initial phase of the carcinogenesis appeared to be constituted by the rapid proliferation of "oval cells" which then could degenerate into one of the different types of carcinomas. Invasion of the intrahepatic veins was also seen in the latter stages of the development of the tumor. In a parallel series of experiments where dimethylaminoazobenzene was fed for 2-4 mo., it was found that there were some close morphological analogies between the various phases of tumor development in the two experimental conditions.

64-2111 INTERACTION OF NUCLEIC ACIDS. I. PHYSICAL BINDING OF THYMINE, ADENINE, STEROIDS, AND AROMATIC HYDROCARBONS TO NUCLEIC ACIDS. (E.) Ts'o, P. O. P. (Johns Hopkins U., Baltimore, Md.) and P. Lu. Proc. Nat. Acad. Sci. USA 51(1):17-28, 1964.

The affinity constants (n_k ; where n = no. of binding sites and k is the av. association constant of each site) between certain compounds and nucleic acids were measured by equilibrium dialysis at 5°C in buffered soln. (0.5 M salt). The order of the increasing n_k of these compounds to the nucleic acids was: thymine << adenine, caffeine < naphthalene < diethylstilbestrol < estradiol- β -17 < testosterone < phenanthrene. The n_k of the nucleic acids in coil form was

much higher than those in the helical form. DNA showed a 2-order of magnitude higher n_k than RNA. Nucleic acids tested were native and heat-denatured thymus DNA, helical poly A and coil poly A, poly U, ribosomal RNA, as well as yeast sRNA.

64-2112 THE EFFECT OF COPPER ACETATE ON BIOCHEMICAL CHANGES INDUCED IN THE RAT LIVER BY p-DIMETHYLAMINOAZOBENZENE. (E.) Fare, G. (Dept. Path., U. Birmingham Sch. Med., England) and D. L. Woodhouse. Brit. J. Cancer 17(3):512-523, 1963.

When cupric oxyacetate hexahydrate (CuAc; 0.5%) was added to the maize diet (M) of female rats in addition to dimethylaminoazobenzene (DAB; 0.09%), the biochemical changes associated with the latter were delayed, but not eliminated. There were some limits on the extent of changes in the absolute amounts and distributions among the subcellular fraction of protein, RNA, DNA and succinoxidase activity in the liver. When DAB was fed alone, succinoxidase activity fell below the normal range before tumors developed and the copper content in the liver increased by 35%. When CuAc was added to the basic M diet, Cu liver storage increased 200x normal after 380 days. When both CuAc and dye were fed, copper storage in the liver was 40x normal. These findings are in accord with the fact that Cu delays, but does not prevent cancer of the liver in DAB-fed rats. For an earlier study, see CRA 1(11):#1918, 1964. See also CRA 1(12):#2061, 1964.

64-2113 INDUCTION OF THYROID TUMORS IN RATS TREATED WITH PROPYLTHIOURACIL AND RADIOACTIVE IODINE. (Fr.) Stoll, R. (Dept. Biol., Bergonié Found., Bordeaux, France) and R. Maraud. Bull. Assn. Franc. Cancer 50(3):389-398, 1963.

In male Wistar rats, neither a s.c. inj. of 30 μ C radioactive iodine at 9 mo. of age nor admin. of propylthiouracil (PTU; p.o.) for 1, 3, or 6 mo. alone induced malignancies, although PTU increased the frequency of benign adenomas (compared to controls). When ¹³¹I was admin. to animals aged 9 mo. and following 1 mo. of treatment with PTU, no carcinogenic effect was evidenced; however, when given after 3 or 6 mo. of PTU, 5/18 animals developed massive, highly invasive, polymorphous carcinomas of the thyroid (1 metastatic to the lung), with a latent period of 6-15 mo. The authors conclude that admin. of ¹³¹I is probably contraindicated in pts. who have been treated previously with thyroid suppressants. This would especially be true in the case of young pts., in view of the relationship of the indicated latent period to the life span of the experimental animals.

64-2114 STUDIES OF INDUCED PROLIFERATIONS IN MICE. I. CYTOLOGIC EFFECTS OF THE APPLICATION OF 3,4-BENZOPYRENE ON EPIDERMAL PROLIFERATIONS INDUCED BY GRAFTS OF EMBRYONAL LUNG

FRAGMENTS. (Fr.) Bouchard, J. (Lab. Compar. Anat., U. Paris Sorbonne, Sch. Med., France) and R. M. May. Bull. Assn. Franc. Cancer 50(3): 423-446, 1963.

In Swiss albino mice bearing homologous grafts of embryonal pulmonary tissue, a single, topical application of 3,4-benzpyrene significantly increased epidermal proliferations as compared to controls bearing grafts alone or treated with the agent alone. The mitotic index was also increased temporarily, as was the onset of keratinization and the number of mitotic anomalies occurring at anaphase. No malignancies were induced.

64-2115 SEQUENCE OF EARLY IMMUNOLOGICAL CHANGES IN THE COURSE OF CANCERIZATION BY MEANS OF DIMETHYLAMINOAZOBENZENE. (Fr.) Dufour, D. (Dept. Biochem., U. Laval Sch. Med., Quebec, Canada) and J.-M. Boucher. Rev. Franc. Etud. Clin. Biol. 8(8):789-792, 1963.

In Sprague-Dawley rats weighing 200 g at the beginning of the experiment, 4-diethylaminoazobenzene, added to the basic diet, failed to induce any immunoelectrophoretic changes in the serum, spleen or liver over a period of 8 wk. In rats receiving dimethylaminoazobenzene (also p.o.), no changes were demonstrable at the end of wk. 4 or 5. After 6 wk., however, a scission of the serum albumin immunoelectrophoretic precipitation line was evidenced in 4/20 rats; this appeared in 9/14 by the 8th wk. and was followed 2 wk. later, by a marked elongation of the splenic precipitation line on the positive side. There was no direct relationship between the amount of dye ingested and the appearance of these changes; each animal appears to possess a highly individualized threshold of sensitivity to the carcinogen, some showing changes after having ingested 189 mg of azo dye while others show no changes after ingestion of 354 mg. (For correlative studies see CRA 1(2): #199; ibid., (3):#444; ibid., (8):#1512, 1963; and ibid., (11):#1927, 1964.)

64-2116 EPITHELIAL TUMORS OF THE STOMACH INDUCED IN GUINEA PIGS BY INTRAMURAL INJECTION OF 3-METHYLCHOLANTHRENE. (Sp., Abstract) Zaldivar, R. S. d. (Dept. Biol., U. Chile Sch. Med., Santiago), C. Aliaga and H. Rodríguez. Acta Physiol. Lat. Am. 12(2):220, 1963.

A total of 14 male and 11 female guinea pigs received 20-methylcholanthrene (MC; 1 mg in 0.05 ml polyethylene glycol-400), by single inj. into the ventral wall of the gastric antrum. During an observation period of 8 mo., gastric epithelial tumors developed in 14/25: 10 diverticula (1 invading the contiguous muscle sheath) and 4 infiltrating epithelial lesions. Two of the animals with neoplasms also showed localized mucosal hyperplasia. No effect was obtained when the polyethylene glycol-400 alone was used. For effects of implantation of crystals of MC, see CRA 1(12):#2117, 1964.

64-2117 GASTRIC LESIONS INDUCED IN THE GUINEA PIG BY INTRAMURAL IMPLANTATION OF CRYSTALS OF 3-METHYLCHOLANTHRENE. (Sp., Abstract) Zaldivar, R. S. d. (Dept. Biol., U. Chile Sch. Med., Santiago), C. Aliaga and H. Rodríguez. Acta Physiol. Lat. Am. 12(2):217, 1963.

A total of 21 male and 20 female guinea pigs received 3-methylcholanthrene crystals (3 mg) by single implant into the ventral wall of the gastric antrum. During an observation period of 515 days, gastric epithelial lesions appeared in 14/41 animals. Induced were 11 diverticula (1 accompanying an infiltrative epithelial lesion and 2 showing beginning invasion of the adjacent muscle sheath), 3 additional infiltrative epithelial lesions, 2 instances of precancerous changes, 1 gastric leiomyosarcoma, and 1 s.c. fibrosarcoma without metastasis. There was no relationship between sex and tumor incidence. (See also CRA 1(12):#2116, 1964.)

64-2118 THE ROLE OF CRYPTORCHISM IN THE DEVELOPMENT OF TESTICULAR TUMORS. (Fr.) Zimel, H. (C. I. Parhon Inst. Endocr., Acad. Sci. Rumania, Bucharest) and A. Măcrineanu. Rev. Sci. Med. (Bucur.) 8(3/4):197-199, 1963.

In adult, male, albino Wistar rats, intra-abdominal fixation of 1 or both testicles prior to or concomitant with intratesticular implant of homologous tumors (methylcholanthrene-induced sarcoma, Walker carcinosarcoma 256, or Guerin carcinoma) increased tumor takes from 70 to 100% and increased tumor vol. by approx. 250%, as compared to the implanted, non-fixed, contralateral testicle or the testicle of implanted controls. The extent of invasive tumor growth, and both local and distant metastasis, were also increased significantly. All effects were demonstrable only so long as the testicle was kept ectopic and ceased upon restoration of the testicle to a scrotal position. All were suppressed by prior hypophysectomy, although concurrent treatment with testosterone did not modify them. Tumor implants made after restoration of the testicle to a scrotal position behaved exactly as did those in controls; although chronic irritation of the nerves of the spermatic cord, in rats with normally placed testicles, had the same effect as ectopy. The authors conclude that diminution of testicular secretion of androgen and increased pituitary gonadotropic activity in cryptorchidism, are not the only elements responsible for an increased tendency to tumefaction, but that both chronic traumatization and the increased temperature within the abdomen also play a very important role.

64-2119 CARCINOGENESIS IN LEWIS RATS INJECTED AT BIRTH WITH 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Toth, B. (Inst. Med. Res., Div. Oncology, Chicago Sch. Med., Ill.) and P. Shubik. Brit. J. Cancer 17(3):540-545, 1963.

Among newborn Lewis rats given 9,10-dimethyl-1,2-benzanthracene (DMBA; s.c. interscapularly dissolved in 0.05 ml tri-n-caprylin (TC)) in doses of 1,000, 100, 75, and 25 µg, the percentage of survivors at weaning with s.c. sarcomas was, resp., 75%, 17.3%, 7.8% and 5%. The number of survivors at the time of weaning was 12/119 for 1000 µg DMBA, 16/112 for 100 µg, 37/58 for 75 µg, 24/45 for 50 µg, 40/88 for 25 µg, 20/116 for 10 µg, and 24/118 for TC-inj. controls. No tumors were found in rats given 50 and 10 µg DMBA nor in TC- or untreated controls. The latent period increased from 7-33 days to 72-81 days with decreasing dose of DMBA. Histologically the tumors were spindle cell sarcomas and some areas showed hemangiomatous or hemangiosarcomatous features with only one lung metastasis reported. Other tumors were found in both treated and untreated rats but were not believed related to the treatment. See also CRA (4):#657, 1963.

4-2120 MALIGNANT TUMORS OF THE THYROID. ANATOMICAL-CLINICAL STUDY OF 155 CASES FROM PORTUGAL. (Por.) Silveira Botelho, L. da. Portugese Inst. Of Oncol., Lisbon). Arq. Pat. 5(3):243-456, 1963.

After a review of some of the literature on the frequency of cancer of the thyroid in various countries and in relation to age, race, geographic location, carcinogenic factors and the presence of simple goiter, an anatomical and clinical study is reported on 155 cases occurring in Portugal. Only 11/155 cases were born in zones of endemic goiter; only 2 pts., with an initial diagnosis of thyrotoxicosis, took thio derivatives for a period

of time. In 2/7 cases of thyroid tumors in childhood there was a history of exposure to radiations. The experimental production of thyroid tumors is also reviewed. The inj. of 2 mg of acetylaminofluorene (AAF) for a period of 4 mo. (no details) resulted in macroscopic increase in the thyroid gland in 7/30 hemithyroidectomized white rats subjected to autopsy, compared to 4/22 controls (hemithyroidectomized). The admin. of 2.5 mg AAF for 1 wk. after hemithyroidectomy, followed by p.o. admin. of methylthiouracil for the duration of survival, resulted in thyroid augmentation in 18/45 animals verified at autopsy. The admin. of a diet free of iodine, containing methylthiouracil (4 g/2 kg of meal) caused hypertrophy in 18/18 animals. Histologically, only in the last group were there carcinomas, predominantly solid, although the group that received AAF + methylthiouracil showed well defined nodules.

64-2121 MORPHOLOGY OF LIVER TUMORS INDUCED IN THE MOUSE AND IN THE GUINEA PIG BY THE ADMINISTRATION OF DIETHYLNITROSAMINE. (Ger.) Thomas, C. (Inst. Path., U. Bonn, Germany) and D. Schmähl. Zschr. Krebsforsch. 65(6):531-536, 1963.

In guinea pigs, admin. of diethylnitrosamine (3-5 mg/kg/day, total dose 1200 mg/kg, p.o.) resulted in the development of liver cell carcinomas. In DBA mice malignant hemangioendotheliomas developed after daily doses of 13 mg/kg, with a total dose of 2340 mg/kg. Thus the severity of the tumor-inducing effect of the agent was dependent not only on the amount of the daily dose, but also on the species of animal.

See also abstract nos.: 2045, 2053, 2061, 2065, 2071

VIRAL CARCINOGENESIS

- 64-2122 FURTHER INVESTIGATIONS ON ANTIGEN DIFFERENCES BETWEEN TISSUES OF VIRUS-INDUCED MYELOID AND LYMPHATIC LEUKEMIAS OF THE MOUSE. (Ger.) Pasternak, G. (Inst. Exp. Cancer Res., German Acad. Sci., Berlin, Berlin-Buch), K.-H. Horn and A. Graffi. Acta Biol. Med. German 11(2):293-297, 1963.

Pretreatment of mice with homologous transplants of several different spontaneous or transplantable strains of lymphatic leukemia did not succeed in immunizing them (inducing resistance) to isologous transplants of 3 strains of myeloid leukemia: resistant animals, experimental 17/111 (15.3%), controls 21/88 (23.9%). Reciprocal experiments, attempting to induce in mice resistance to isologous transplants of a viral lymphatic mouse leukemia by pretreatment of the mice with homologous transplants of virus-induced myeloid leukemias, were also negative: resistant animals, treated 3/37 (8.1%), controls 2/29 (6.9%). Despite the negative results of attempts to induce cross resistance between lymphoid and myeloid mouse leukemias, however, preliminary experiments attempting to induce in mice resistance to isologous transplants of myeloid mouse leukemia by pretreatment with heterologous transplants of a lymphatic rat leukemia showed a slight immunizing effect of the heterologous (rat) leukemic tissue: resistant animals, treated 22/33 (66.7%), controls 23/63 (36.5%) = $P < 0.005$. Should this apparent cross reactivity between lymphatic rat leukemia and myeloid mouse leukemia be confirmed, it would signify that a single kind of virus could induce leukemias of different cell types; also, that the specific antigens produced are to a great extent identical, independent of the host species.

- 64-2123 INVESTIGATIONS ON THE PERSISTENCE OF TUMOR-SPECIFIC ANTIGENS IN METHYL-CHOLANTHRENE-INDUCED MOUSE SARCOMAS AFTER VARIOUS TRANSPLANTATION PASSAGES IN ISOLOGOUS HOSTS AND IN F₁-HYBRIDS. (Ger.) Horn, K.-H. (Inst. Exp. Cancer Res., German Acad. Sci. Berlin, Berlin-Buch), G. Pasternak and A. Graffi. Acta Biol. Med. German 11(2):298-302, 1963.

Inbred line XVII mice and their hybrids with CBA (F₁), immunized against the methylcholanthrene (MC)-induced sarcoma 1283 by inj. of irradiated tumor tissue, when challenged with MC 1283 tumor cells (10^5 or 5×10^4 cells), showed 10/21, 11/29, and 19/28 resistant animals, resp., in transplant generations 1-4, 5-9, and 9-22 (controls, 0/20, 0/19, and 1/20). Line XVII inbreds, similarly immunized and tested against sarcoma MC 1123 tumors, showed similar maintenance of resistance over 13 transplant generations (4/5, 5/17, and 11/17 resistant animals in generations 1, 8, and 13, resp.; controls 0/5, 0/13, 2/9). Response to a third tumor type differed. Though resistance to sarcoma MC 2395 was high in transplant generation 1 of line XVII mice (20/21 and 18/18

resistant animals after immunization by inj. irradiated tumor tissue or by ligation of intradermal tumor, resp.; controls 11/45), in generations 21 and 34 after similar immunizations only 1/13 and 1/18 resistant animals appeared, resp. (0/25 controls). Thus, resistance to tumor MC 2395 was lost during various passages, while resistance to tumors MC 1283 and MC 1123 was maintained through many passages. In another series of experiments, where F₁ mice of XVII female x CBA male were immunized against sarcoma MC 1283 tumors, the induced resistance to tumor specific antigens was not materially changed, whether the hosts were challenged by tumors maintained during 12 passages in the original XVII strain or in the F₁ hybrids.

- 64-2124 ELECTRON MICROSCOPIC STUDY OF THE PASSAGE A MOUSE LEUKEMIA VIRUS IN MAMMARY GLANDS OF PREGNANT, VIRUS-INJECTED, C3H(f) MICE. (E.) Feldmah, D. G. (VA Hosp., Bronx, New York), L. Gross and Y. Dreyfuss. Cancer Res. 23(9):1604-1607, 1963.

Ultrathin sections of mammary glands from 4 pregnant C3H(f) mice with passage A virus-induced leukemia contained numerous particles similar in appearance to those observed in the organs of leukemic donor mice. The particles often seemed continuous with the cell membrane of the mammary epithelium, apparently in the process of budding. Examination of the glands of pregnant virus-injected but non-leukemic mice showed similar particles, but in smaller amounts, in 3/5. No particles were observed in the mammary glands of 3 pregnant and 2 lactating non-inoculated controls. Many of the particles found in these studies had two concentric membranes and an electron-lucent center and others had a large, centrally located nucleoid of variable density whereas some of the extracellular particles found in mice carrying the mouse mammary carcinoma virus have four concentric membranes and others have a dense eccentric nucleoid.

- 64-2125 LDH LEVELS IN BLOOD AND TISSUES OF MICE INFECTED WITH AN LDH AGENT. (E.) Bailey, J. M. (Dept. Biochem., George Washington U. Sch. Med., Washington, D. C.), M. Stearman and J. Clough. Proc. Soc. Exp. Biol. Med. 114(1):148-153, 1963.

An agent, similar to that described by Riley and which causes a rapid rise in plasma lactic dehydrogenase (LDH), was found in 2 transplantable mouse tumors (CD/5 lymphoma and DBA/59 mammary carcinoma). When LDH activity was determined in tissues (brain, heart, kidney, liver, lung, thymus, pancreas, skeletal muscle, spleen, submaxillary gland), no significant differences were found in those of normal and LDH factor-infected mice. Hematocrit values were slightly but significantly lower than normal in mice bearing the LDH agent.

64-2126 ROLE OF VIRUSES IN THE ETIOLOGY OF LEUCOSES. (E.) Mazurenko, N. P. Translation of monograph Rol' Virosov v Etiologii Leukozov, Kiev, 1962, pp. 148-190. Cited in *Arch. Transl.* 10(9):1018, 1963.

Translation of chapters 6 and 7 dealing with the mechanism of smallpox vaccine-induced leukoses in mice and the viral etiology of human leukemias. Full translation available from Office of Technical Services, number 63-31284, at a cost of \$1.00.

64-2127 POSSIBLE VIRAL ETIOLOGY OF BOVINE AND EQUINE LEUKEMIA. (E.) McKercher, D. G. J. California Sch. Veterin. Med., Davis), E. M. Sada, O. C. Straub and G. H. Theilen. *Ann. N. Y. Acad. Sci.* 108(Art. 3):1163-1172, 1963.

Three isolations of virus were made in California from lymph node, blood and milk, resp., of a leukemic cow, and 1 from the lymph node of a leukemic horse but not from corresponding tissues of non-leukemic cattle. The bovine lymph node isolate and the equine isolate were partially characterized in tissue culture studies and studies in embryonated eggs, mice and calves. These 2 isolates showed some serological similarities with an isolate recovered in Italy from lymph node of a leukemic cow.

64-2128 RESEARCHES ON A VIRUS ISOLATED FROM A CALF AFFECTED WITH LYMPHATIC LEUKEMIA. (E.) Papparella, V. (Inst. Infect. Dis., Sch. Veterin. Med., Naples, Italy), A. Cali, G. B. Cusi and A. Iacobelli. *Ann. N.Y. Acad. Sci.* 108(Art. 3):1173-1192, 1963.

Further observations are reported on a virus originally isolated from a calf with lymphoid leukemia (see CRA 1(5):#941, 1963). Of 107 newborn Swiss mice inj. i.p. with 0.1 ml of viral material obtained from the 11th and 12th passages of calf kidney tissue cultures, after 1 yr. 22 had breast tumors, compared to 5/102 inj. with inactivated virus and 2/34 in untreated controls. Attempts to recover the virus directly from the tumors have been unsuccessful. Calves 8 inj. as newborns with various viral materials, after approx. 2 yr. showed no significant pathological changes compared to controls. The lymph nodes of 14/18 showed histological changes such as thicker cortex, fewer (sometimes absent) follicles and the disappearance of the border between cortex and medulla.

64-2129 ETIOLOGICAL STUDIES ON BOVINE LYMPHOSARCOMA. (E.) Dutcher, R. M. (South Jersey Med. Res. Found., Camden, N. J.), Szekely, E. P. Larkin, L. L. Coriell and R. Marshak. *Ann. N.Y. Acad. Sci.* 108(Art. 3):1199-1162, 1963.

Efforts to isolate and transmit an agent inducing

bovine lymphosarcoma, by means of chick embryo systems or the inj. of material derived from clinically ill animals into other cattle or into different animal species, were not successful. In material obtained from cattle with lymphosarcoma, there appeared to be a toxic material which caused early and hemorrhagic death of chick embryos. After 3 yr. of observation, none of the cattle which had been used for transmission studies (offspring of lymphosarcomatous animals and animals receiving inj. at birth of materials derived from lymphosarcomatous animals) had developed the disease. Cytoplasmic and perinuclear changes were observed in cultured cells derived from cattle with lymphosarcoma. These changes consisted mainly of syncytial-like structures or giant cells, and resembled the cytopathic effect of parainfluenza-3 virus on tissue culture cells. Tissue cultures derived from "normal" animals were found to be susceptible to vesicular stomatitis virus, while 12/16 cultures derived from lymphosarcomatous animals were found to be resistant. In some cases, it was found that fluorescein isothiocyanate-labeled globulins from lymphosarcomatous animals combined specifically with some cytoplasmic components in cultured lymphosarcoma cells, but not with a culture derived from a normal lymph node.

64-2130 VIRUS TUMORS OF THE KIDNEY IN FOWL. II. EFFECT OF TWO ONCOGENIC AVIAN VIRUSES ON THE EMBRYONIC CHICKEN KIDNEY. (Fr.) Chouroulinkov, I. (Lab. Exp. Med., Cancer Sci. Res. Inst., Villejuif, Seine, France) and M.-R. Rivi re. *Bull. Assn. Franc. Cancer* 50(2):219-233, 1963.

Embryonic chicken kidneys, 8-14 days old, were deposited directly on the chorioallantoic membrane of host chicken embryos together with 0.04 ml viral suspension or fragments of tumor tissue (in direct contact with the transplanted kidney). After CHF/1 tumor extract, homogenate, and fragments, proliferative growths similar to adult nephroblastoma were seen, resp., in 30%, 45%, and 90% after 19 days' incubation. After similar treatment with Murray-Begg endothelioma extract, homogenate, or lyophilized tumor cells, true papillary adenomas were seen in 80%.

64-2131 MALIGNIZATION OF RAT EMBRYONIC CELLS BY ROUS SARCOMA VIRUS IN VITRO. (E.) Svoboda, J. (Inst. Exp. Biol. Genet., Czech. Acad. Sci., Prague) and P. Ch yle. *Folia Biol. (Praha)* 9(5):329-342, 1963.

Rat fibroblast cultures which had been cultured for at least 32 days before and 34 days after addition of Rous virus preparation gave rise to tumors when inoc. into young rats. Cell-free extracts from the tumors obtained in rats produced tumors in chicks. These tumors could be transplanted to other chicks. Co-cultivation of rat fibroblasts with Rous sarcoma cells in media

where the latter survived for only a limited period led to their conversion to malignant cells which caused tumors in rats; these tumor cells when transferred to chicks gave rise to sarcomas which could be transferred to other chicks by means of cell-free extracts. Neither the tumor in the rat nor the supernatant of cultures in which rat fibroblasts became malignant contained virus oncogenic for chicks. Rat fibroblast cultures which were rendered malignant contained single and three dimensional clusters of spherical cells which had lost their capacity for contact inhibition. These cells had a markedly basophilic nucleus and a narrow margin of cytoplasm; they were never found in normal rat fibroblast cultures. They are considered by the authors as a new morphotype formed as a result of conversion by Rous virus.

64-2132 NOTES ON THE PATHOGENESIS OF HAEMORRHAGIC CYSTIC DISEASE IN RATS CAUSED BY ROUS SARCOMA VIRUS. (E.) Klement, V. (Inst. Exp. Biol. Genet., Czech. Acad. Sci., Prague) and I. Sácha. *Folia Biol. (Praha)* 9(5):343-353, 1963.

Changes leading to hemorrhagic disease in newborn white Wistar rats inoc. with the Schmidt-Ruppin or with the Prague strain of Rous sarcoma (0.3 ml s.c. of a 50% tumor suspension) were studied systematically between days 4 and 82; the first death occurred on day 82. The earliest change after virus admin. was resorption viremia with distribution of the virus throughout the organism. The virus persisted in liver and lymph nodes for 26 and 11 days, resp., without causing pathologic changes. Subsequently in sensitive tissues such as the reticulo-endothelial connective tissue of the lymph nodes and probably in the vascular endothelium virus disappeared, and necrobiotic changes were observed, leading to the formation of pseudocysts. In the lymph node reticulum, these changes included non-autonomous proliferation, disengagement of reticulum cells from the tissues, the formation of reticular macrophages, and a cytopathic effect. The first clearly identifiable cyst was found on day 11.

64-2133 EFFECT OF INTRAPERITONEAL IMPLANTATION IN THE SWISS MOUSE OF DIFFUSION CHAMBERS CONTAINING FRAGMENTS OF MAMMARY OR OF LEUKEMIC TISSUES OF THE PS STRAIN. (Fr.) Mouriquand, C. (Dept. Histol., U. Grenoble, France), J. Mouriquand and D. Alix. *Nouv. Rev. Franc. Hemat.* 3(5): 619-623, 1963.

Male and female Swiss mice were implanted with chambers containing mammary tumors or fragments of leukemic organs from PS mice. Ten mice died during the experiment and 15 were living and well 10 mo. after introducing the chamber. Examination of 30/55 animals revealed 7 malignant plasmacytoses (2/7 from mammary, 5/7 from leukemic PS tissues); 4 plasmacytoses of questionable

malignancy (2 from mammary tumor implants, 2 from leukemic implants); and 4 benign plasmacytoses (2 from mammary tumor implants and 2 from leukemic implants). In addition, there were 1 reticular lymphosarcomatosis from a lymphosarcomatous fragment, 1 malignant myeloblastic infiltration of liver and spleen from a mammary tumor fragment, and also 2 fibrosarcomas and 1 reticular lymphosarcoma, all from leukemic fragments. No correlation could be found between the malignancies developing in the mice, and the changes occurring in the tumor fragments inside the diffusion chambers. The small pore size (av. 0.45 μ) of the diffusion chamber membranes precludes direct cell transfer, and the results are in agreement with those obtained with cell-free tumor extracts (see CRA.1(3):#584, and *ibid.* (4):#718, 1963). However, the high frequency of plasmacytic change observed in the present study suggest a possible hyperimmune phenomenon which occurs under conditions found in the diffusion chambers.

64-2134 SPECIFICITY OF CHROMOSOME DAMAGE FOLLOWING VIRAL INFECTION. (E., Abstract) Stich, H. (Dept. Biol., U. Texas M. D. Anderson Hosp., Houston) and T. C. Hsu. *J. Cell Biol.* 19(2):67A-68A, 1963.

A study was made of the effect of various viruses (including a virulent and attenuated strain of herpes simplex (HS), herpes zoster, adenovirus 12 and 18, and SV40) on the chromosomes of classic diploid male and female lines of Chinese hamster and a line of diploid human lung. After HS, the distribution of chromosome gaps and breaks followed a nonrandom pattern also seen after treatment of cells with 5-bromodeoxyuridine; the effect of the other viruses appeared to be random and comparable to the chromosome damage produced by ionizing radiation.

64-2135 POLYKARYOCYTOSIS INDUCED BY ROUS SARCOMA VIRUS IN CHICK FIBROBLASTS. (E.) Moses, E. (Israel Inst. Biol. Res., Ness Ziona) and A. Kohn. *Exp. Cell. Res.* 32(1):182-186, 1963.

Within 1 wk. after infection of cultures of chick fibroblasts with Rous sarcoma virus (RSV; tumor extract CT 935) polykaryocytes (syncytia) were observed in addition to typical sarcoma cell foci. Each polykaryocyte contained 10 or more nuclei; their cytoplasm stained well with supravital cresyl blue. Both the production of polykaryocytes and of foci was neutralized to the same extent by anti-Rous turkey serum but not by anti sera prepared against other syncytial viruses such as measles, SV5, and parainfluenza 1, 2 and 3. It is suggested that polykaryocytosis is an alternative, or an additional, more cytopathic effect of RSV than its neoplastic transforming property.

64-2136 POSSIBLE ROLE OF INTERFERON IN DETERMINING THE ONCOGENIC EFFECT OF POLYOMA

VIRUS VARIANTS. (E.) Friedman, R. M. (NCI, Bethesda) and A. S. Rabson. *J. Exp. Med.* 119(1): 71-81, 1964.

Infection of newborn C3Hf/Bi mice with both the highly oncogenic S variant and the poorly oncogenic M variant of polyoma virus caused significantly fewer tumors than infection with the S variant alone. Moreover, infection with either M or S variants caused resistance to infection with the encephalomyocarditis virus, but the M variant gave a somewhat greater degree of resistance. Extracts of tissues from animals infected with the M variant had measurable levels of interferon, reaching a peak about 5 days after virus infection; extracts from animals infected with the S variant showed no interferon activity. The S variant at 5 days after infection showed a 1000-fold higher titer than the M variant, although at 10 days the difference in titer was only 10-fold.

4-2137 NATURAL TRANSMISSION OF LEUKEMIA IN DIFFERENT MOUSE STRAINS. (Sp.)
e Asúa, F. J. (Iturrat Found. Oncol. Res., Buenos Aires, Argentina), E. Rennella and M. L. Fernández. *Rev. Argent. Cancerol.* 4(3):141-148, 1962.

Swiss mice were inoc. i.p. before 24 hr. of age and 3 or 4 more times in the following weeks with cell-free extracts derived from leukemic organs from AK mice. Among 38 offspring in 7 litters where neither parent subsequently developed leukemia 13 mo. after treatment, there was only one case of leukemia (which occurred after 10 mo.). In 3 litters, where only one of the parents developed leukemia, there were no cases of leukemia among 20 offspring. In another 4 litters, where both parents developed leukemia, 7/24 offspring developed leukemia (6 generalized and 1 mycic) between the ages of 5 and 11 mo., with predominance of females (2 males, 5 females). The overall incidence of 29% was 10x the spontaneous rate; however, since one litter showed 3 cases, the incidences in the remaining 3 litters were 40, 50 and 60%. Similar experiments were carried out using cell-free extracts of tissue homogenates derived from isologous animals which developed spontaneous leukemia. Among 18 offsprings in 3 litters in which the parents did not develop leukemia, there were 6 cases of leukemia (2 males, 4 females) which appeared between 3.5-7.5 mo.; one litter was leukemia-free. In a litter where only the male parent became leukemic, incidence of leukemia was 16.6% of 6 while it was 66.6% of 3 in a litter where the female parent was the only one which became leukemic. The authors remark that the number of animals was too small to draw significant conclusions. In 3 litters (18 offsprings) where both parents developed leukemia there were 7 cases of leukemia between 3-13 mo. with incidences of 25%, 25% and 66% in each litter. In an analysis of incidence of spontaneous

leukemia in their Swiss mouse colony the authors found 17 cases of spontaneous leukemia (11 males, 6 females) appearing mainly between 5-6 mo. of age (13/17). There were 2 cases of familial type transmission. A female that died of leukemia at 5 mo. had given birth to 2 males and 1 female. Both males died with large thymomas at 5 mo. of age. In another litter a brother and sister died at 6 mo. of age with complete leukemia. The authors analyze their results in terms of vertical transmission of leukemia.

64-2138 PROPAGATION AND IMMUNOFLUORESCENT INVESTIGATIONS OF FRIEND VIRUS IN TISSUE CULTURE. (E.) Osato, T. (Ruswell Park Mem. Inst., Buffalo, N. Y.), E. A. Mirand and J. T. Grace. *Nature (London)* 201:52-54, 1964.

Primary HA/ICR mouse embryo cultures infected with Friend's leukemia virus (1 ml of a 10% mouse spleen filtrate, $103.4 \text{ ID}_{50}/\text{ml}$) released infective virus into the medium starting on day 5. The viral titer increased slowly through to day 15 to a max. of $10^{1.9} \text{ ID}_{50}/\text{ml}$, and this was followed by a slight decrease on day 20. However, specific immunofluorescence was demonstrable by the indirect technic starting on day 3 in a small number of cells. By day 5 discrete foci of infected cells were visible, but the fluorescence was limited to the perinuclear area of the cytoplasm and involved about 1% of the cells. On day 14 about 10% of the cells showed specific fluorescence, and this involved the entire cytoplasm. There was no evidence of specific nuclear fluorescence or cytopathic changes throughout the period of observation. There was a relative disparity between the quantity of released and intracellular virus, and surface fluorescence was not significant in the system, suggesting that viral antigen synthesis occurs more rapidly than maturation and release of complete virus.

64-2139 GROWTH OF A RETICULUM CELL SARCOMA VARIANT OF FRIEND DISEASE IN THE EMBRYONATED HEN'S EGG. (E.) Dawson, P. J. (Dept. Path., Roy. Victoria Infirm., Newcastle/Tyne, England), A. H. Fieldsteel, W. L. Bostick and S. Smith. *Nature (London)* 201:91-92, 1964.

A reticulum cell sarcoma derived from the tissues of a BALB/c mouse infected with Friend leukemia virus was inoc. into embryonated eggs from Heisdorf and Nelson Leghorn hens mated with California Grey roosters. Implantation of 2-3 mm tumor fragments over the bifurcation of a large vein on the chorio-allantoic membrane of 8-day embryos resulted in definite growth of the explant in 5/63. Apparently viable cells similar to those of the original tumor were present in 42 of the explants and 20/28 of the latter were capable of inducing tumors in 6-8-week-old mice implanted s.c. Also 21 of the explants contained enough virus to produce generalized Friend disease in the mice as judged by microscopic changes in the spleen. Three of the mice

with tumors showed no changes in the spleen; 4 mice showed splenic changes but did not develop tumors. Although examination of the brain, liver, lungs and heart of embryos implanted on the chorioallantoic membrane did not reveal metastatic tumor, bioassay of the organs of 6 of the embryos resulted in Friend disease from suspensions of the brains of 2 and of the spleen from 1 embryo. Inoculation of tumor cells in the yolk sac of 86 embryos resulted in local tumors in only 3/45 survivors. Microscopically metastases were seen in the brain of 2 embryos, and viable virus and/or tumor cells were present in the spleens of all 3 and the livers of 2. Intravenous inoc. of the tumor did not cause gross tumors in 86 survivors (of 207 inoc.), but 33 of these had histologically detectable brain metastases. While there was no histological evidence of tumor in the liver, spleen, heart, or lungs of these embryos, bioassay revealed that 11/21 had metastases to the liver (but none in the spleen). Furthermore, while the brain from 9/11 produced tumors by the bioassay method, 4 of these did not reveal metastatic tumor when single sections were examined microscopically. When 5 embryos were allowed to hatch, when killed at 32 days 3 showed microscopic tumor deposits in the heart, liver, lungs, and spleen but not in the brains.

64-2140 INHIBITION OF VIRUSES BY SECRETIONS FROM THE FEMALE GENITAL TRACT. (E.) Pannu, J. S. (Variety Children's Res. Found., Miami, Fla.) and M. M. Sigel. Proc. Soc. Exp. Biol. Med. 114(3):763-766, 1964.

Human cervicovaginal secretions (CVS; total 229 washings and swabbings) were found capable of inhibiting polio (P), herpes simplex (H) and Rous sarcoma (R) viruses in vitro (for P and H, tissue culture of HeLa or KB cell lines in Eagle's medium with calf serum and examined for cytopathologic effect) and P virus in vivo. CVS-R virus mixtures (hyaluronidase added, 30 USP U/ml) were incub. for 1 hr. at 4°C and 0.05 ml aliquots inoc. onto the chorioallantoic membrane of 9-day-old embryos: all secretion pools caused inhibition of R plaques. Overall, the findings may explain why it was not possible to isolate any virus(es) from the vaginal washings and suggest that at least part of the inhibitory activity is not due to antibody.

64-2141 IN VITRO TRANSFORMATION OF HAMSTER EMBRYO CELLS BY SV40 VIRUS. (Fr.) Thomas, M. (Inst. Leuk. Res., St. Louis Hosp., Paris), J. Tanzer, J.-P. Lévy, M. Boiron and J. Bernard. C.R. Acad. Sci. 257(17):2573-2576, 1963.

Second passage hamster embryo cells infected with SV40 virus and incub. at 37°C for about 3 wk. following infection begin to multiply rapidly and in three dimensions rather than in

monolayers, with rapid acidification of the media. Further passages of the transformed cells do not alter these characteristics and the rapid rate of growth requires passage every 2 days compared with weekly transfers required for control cultures. Microscopic examination showed that the nuclei of transformed cells were irregular in size and that mitoses were numerous and often abnormal. Chromosomal studies revealed a group of cells which showed a hypotetraploid number of chromosomes (78), others had around a hypooctaploid number of 138 and then many more with a greater, but uncountable, number of chromosomes. When 10^6 transformed cells of the 11th or the 21st passage were grafted in the intrascapular region of month-old hamsters, tumors developed in all animals within 8-30 days. No tumors developed when control cells were used. There was no evidence of intracellular inclusions nor could SV40 virus be recovered from the transformed cells.

64-2142 IMMUNITY IN HAMSTERS TO CELLS TRANSFORMED IN VITRO AND IN VIVO BY SV40. TESTS FOR ANTIGENIC RELATIONSHIP AMONG THE PAPOVAVIRUSES. (E.) Khera, K. S. (Dept. Virol., Baylor U. Coll. Med., Houston, Tex.), A. Ashkenazi, F. Rapp and J. L. Melnick. J. Immun. 91(5): 604-613, 1963.

Inoculation of SV40 into hamsters 3-4 wk. prior to challenge with approx. 10^2 - 10^4 SV40-transformed cells (in vitro or in vivo) led to either no tumor growth or increased latency in the resistant animals. When tumors developed they were generally smaller than those in controls. Results were similar when the tumor cells were inoc. s.c. into the cheek pouch, or intracerebrally. This resistance was not due to antiviral antibody. Heat-inactivated virus did not confer protection. Ruptured transformed cells conferred a lesser degree of resistance in hamsters. Polyoma virus gave no protection. Human wart virus and Shope papilloma virus seemed to produce a limited degree of protection.

64-2143 INCOMPLETE SIMIAN PAPOVAVIRUS SV40. FORMATION OF NON-INFECTIOUS VIRAL ANTIGEN IN THE PRESENCE OF FLUOROURACIL. (E.) Melnick, J. L. (Dept. Virol., Baylor U. Coll. Med., Houston, Tex.), S. E. Stinebaugh and F. Rapp. J. Exp. Med. 119(2):313-325, 1964.

Both 5-fluorouracil (FU) and 5-fluorodeoxyuridine (FUDR) markedly suppressed the production of new infectious virus by SV40-infected cercopithecus monkey kidney cells. Synthesis of viral protein was markedly suppressed by FUDR, but not by FU. Infected cells in the presence of FU produced large amounts of viral protein; the antigen was not distributed in a particulate fashion as in untreated cells. Distribution of virus antigen was diffuse in the nuclei of FU-treated cells, resembling that of antigen near the end of the eclipse period in untreated, infected cultures.

This stage of antigen production presumably preceded viral assembly. Upon electron microscopy, virus particles with or without cores were rarely seen in infected FU-treated cells, although large numbers of SV40 particles were readily visualized in untreated infected cells. It appears that at least one antigenic protein of SV40 is synthesized abundantly in FU-treated cells, but is not assembled into virus shells in the presence of the inhibitor.

- 64-2144 TRANSFORMATION OF PROPERTIES OF AN ESTABLISHED CELL LINE BY SV40 AND POLYOMA VIRUS. (E.) Todaro, G. J. (Dept. Path., New York U. Sch. Med., N. Y.), H. Green and B. D. Goldberg. *Proc. Nat. Acad. Sci. USA* 51(1): 66-73, 1964.

An aneuploid mouse fibroblast line 3T3 was developed which is very sensitive to contact inhibition of cell division and is virtually unable to synthesize collagen. On infection with the SV40 or with the polyoma virus the cell cultures lost susceptibility to contact inhibition and also to have re-acquired the ability to synthesize collagen. Both changes appeared due to a virus-induced release of latent cellular properties. In addition, after SV40 transformation, cells toward the center of the colonies became rounder in shape, more closely packed and appeared epithelioid. Polyoma virus-transformed cultures showed increased interlacing of cells, looser packing, and absence of an epithelioid pattern, and also consistently produced more acid than the SV40-transformed cultures.

- 4-2145 RECOVERY OF VIRUS FROM THE BLOOD OF RATS WITH INDUCED LEUKAEMIA. (E.) Dalton, A. J. (NCI, Bethesda) and J. B. Moloney. p. 385-392 in *The Interpretation of Ultrastructure*. Symposia Internatl. Soc. Cell Biol. vol. I. Harris, R. J. C. (Ed.). Academic Press Publ.), New York. 438 pp., 1962.

method is described for obtaining by differential centrifugation pellets of relatively pure virus particles from the blood of Osborn-Mendel rats with leukemia induced with the Moloney agent. Electron microscopic examination of the pellets revealed little or no cellular debris, with the exception of a few fibrin-like strands. Many of the particles obtained in the high speed centrifugate possessed narrow projections, similar to those present extracellularly in tissues of rats and mice killed in the late stages of the disease. Preliminary biological tests indicate that 10 wk. after inoc. with a 10^{-1} dilution of the pelleted material 64% of the mice and 88% of the rats have died with leukemia or present macroscopic evidence of the disease.

- 2146 AN ELECTRON MICROSCOPIC STUDY OF THE CHICK EMBRYO PANCREAS FOLLOWING NATURAL

AND ARTIFICIAL TRANSMISSION OF AVIAN TUMOR VIRUSES. (E., Abstract) Zeigel, R. F. (NCI, Bethesda), B. R. Burmester and F. J. Rauscher. *J. Cell Biol.* 19(2):76A, 1963.

In a continuation of previous studies suggesting that the pancreas may be the site of synthesis of the avian lymphomatosis virus, line 151 embryos on the 6th or 10th day of incub. were inoc. with pancreas extracts from embryos presenting the suspected virus particles on electron microscopic examination. Examination on the 19th day of incub. or 11 days after hatching showed the suspected virus particles in 12/13 embryos inoc. with positive pancreas extracts, but in 0/26 inoc. with negative pancreas extracts. Inoculation of embryos with the RPL12 virus yielded particles in the pancreas of 17/20. In parallel but still incomplete studies, a high incidence of lymphomatosis was observed in chicks inoc. with the positive pancreas extracts.

- 64-2147 VIRUS MULTIPLICATION AND CELL KILLING IN POLYOMA-INFECTED MOUSE EMBRYO CULTURES. (E.) Weisberg, R. A. (Hammersmith Hosp., London, W.12). *Virology* 21(4):658-661, 1963.

When mouse embryo cultures were exposed to high conc. of purified polyoma virus, and single cells were subsequently isolated and examined for virus production, it was found that only a small proportion of the cells produced virus. The virus producing cells, however, could liberate about 500 PFU of virus. The proportion of virus producing cells in infected cultures at various input multiplicities of infection was determined by the infective center (IC) technic. In several experiments with input multiplicities of more than 0.1 the proportion of IC was consistently less than expected, although variability occurred among experiments. The highest proportion of IC was 60%, indicating that some of the cells have a lower than av. probability of registering as IC after exposure to the virus. Comparison of the efficiency of plating of infected and uninfected cultures showed that the proportion of cells killed was also lower than expected, with 20-30% of the clone-forming cells surviving at multiplicities of 100-500 PFU/cell. Thus the surviving fraction of mouse embryo cultures has a lowered probability of undergoing a cytotoxic interaction with polyoma virus. Other data published elsewhere on the susceptibility of infection of clonal lines, and on the reinfectability of cultures derived from surviving fractions suggest that such a fraction is not the result of a mutational event, but rather is due to transient physiologic fluctuations in the susceptibility of the cells to the cytotoxic effects of the virus.

- 64-2148 DELAYED APPEARANCE OF TRANSFORMED CELLS IN POLYOMA VIRUS-INFECTED MOUSE EMBRYO CULTURES. (E.) Weisberg, R. A. (Hammersmith Hosp., London, W.12). *Virology* 21(4):669-671, 1963.

When cultures of mouse embryo cells were exposed to polyoma virus at input multiplicities of infection of 5 PFU/cell and the cultures were then cloned at various times after infection, the first transformed cells were detected usually 4-5 wk. after infection. Similar results, but accompanied by extensive cell degeneration, were obtained on infection with multiplicities of up to 5000 PFU/cell. Experiments designed to demonstrate destruction of early arising transformed cells by cytotoxic action, delayed expression of the transformed character, or presence of a low frequency of preexisting transformable variants were unsuccessful.

- 64-2149 THE CORTICOID-TRANSFORMING CAPACITY OF VARIOUS ORGANS IN EXPERIMENTAL VIRUS LEUKEMIA. (Hun.) Tuzson, P. (Dept. of Physiol. Pathophysiol., Nat. Inst. Health, Hungary) and P. Kertai. Magy. Onkol. 7(2):114-121, 1963.

Hydrocortisone (H) transformation in normal Leghorn chicken spleen and liver slices was compared with that in slices from chickens with virus erythroblastosis. Equivalent amounts of tissue (about 0.5 g) were incub. in Krebs-Ringer soln. for 3 hr. at 37°C. Under these conditions, tissue from the greatly enlarged spleens of the leukemic chickens transformed twice as much H (59.9%) as spleen tissue from normal chickens (22.8%); given the 4x increase in the wt. of the spleen in the leukemic fowl, this indicates an 8x increase in the metabolic rate in erythroblastosis. Normal liver tissue transformed 47.0% of the H present, as against 56.4% transformation by liver tissue from the chickens with erythroblastosis; here the increased metabolism is proportional to the increased liver wt. in the latter (av. 5.35 g, as against 3.15 g in controls). Phenylbutazolidine blocked the *in vitro* metabolism of H in spleen tissue from both normal and leukemic chickens. *In vivo*, however, although virus-inoc. chickens given phenylbutazolidine, H, or both did not develop splenomegaly, they lived no longer than untreated controls, and the enhanced hydrocortisone-transforming capacity characteristic of the disease was not inhibited.

- 64-2150 RESULTS OF MEASURES TAKEN TO CONTROL AND ELIMINATE BOVINE LEUKOSIS. (Ger.) Bendixen, H. J. (Serol. Lab., State Inst. Veterin. Med., Copenhagen). Berlin. Munchen. Tieraerztl. Wschr. 76(16):329-331, 1963.

The incidence of bovine leukosis (per 100,000) on the islands of Sjoelland and Lolland-Falster (Denmark) declined gradually from 15 in 1953-54 to 14 in 1959, in response to a government-sponsored program of destruction of all infected animals; then rose abruptly to 29 in 1960. Total destruction of all herds containing infected animals, with replacement by animals from areas free of the disorder, brought the incidence down to 21 in 1961 and 17 in 1962. Meanwhile, incidence

of the disorder on Jylland, Fyn, and Bornholm, with a bovine population of approx. 3,000,000 (as opposed to ½ million on the other 2 islands) remained constant throughout the entire period at approx. 1.0-1.5/100,000. The authors conclude that the disorder is infectious in nature.

- 64-2151 PREVENTIVE MEASURES IN CATTLE LEUKEMIA: LEUKOSIS ENZOOTICA BOVIS. (E.) Bendixen, H. J. (Govt. Veterin. Serum Lab., Copenhagen). Ann. N.Y. Acad. Sci. 108(Art. 3):1241-1267, 1963.

See CRA 1(12):#2150, 1964. Additional data on the incidence and distribution of the bovine leukoses are presented.

- 64-2152 ELECTRON-MICROSCOPIC DEMONSTRATION OF VIRUS-LIKE PARTICLES IN THE 20-METHYL-CHOLANTHRENE-INDUCED RF MOUSE LEUKEMIA AND ITS CELL-FREE TRANSMISSION. (Jap.) Hiraki, K. (Dept. Int. Med., Okayama U. Sch. Med., Japan), S. Irino, Z. Ota and T. Sezaki. Igaku To Seibutsugaku (Med. Biol.) 66(4):191-198, 1963.

See CRA 1(9-10):#1702 and #1758, 1964. For earlier work see CRA 1(8):#1467, 1963.

- 64-2153 ELECTRON-MICROSCOPIC DEMONSTRATION OF VIRUS PARTICLES IN X-RAY-INDUCED RF MOUSE LEUKEMIA AND ITS CELL-FREE TRANSMISSION. (Jap.) Irino, S. (Dept. Int. Med., Okayama U. Sch. Med., Japan), Z. Ota and S. Sota. Igaku To Seibutsugaku (Med. Biol.) 67(3):162-168, 1963.

The cell-free filtrates of the liver, spleen, thymus and lymph nodes of RF mice with X-ray-induced leukemia, when inj. s.c. into 16-hour-old mice of the same strain, led to the development of lymphatic leukemia in 4/16 (1 thymic, 3 non-thymic) after 1-2 yr. A filtrate made from the tissues of one of 2 mice among 300 which showed spontaneous leukemia, when inj. into newborn RF mice led to development of lymphatic leukemia in 1/12 after 7 mo. When tumor cells of the liver, spleen, lymph nodes and thymus of mice with X-ray-induced leukemia were employed, 59/83 (71.1%) of the inj. mice developed leukemia and survived 20-78 days. Upon electron microscopic examination, virus particles were found in the lymph nodes of mice with X-ray-induced leukemia which were similar to particles described in other leukemias. It is concluded that the occurrence of leukemia could be due to the activation of a virus by the X-irradiation. (For an earlier study, see CRA 1(7):#1343, 1963.)

- 64-2154 INTRACITOPLASMIC VIRUS-LIKE PARTICLES IN HUMAN CHLOROBLASTIC LEUKEMIA AS REVEALED BY ELECTRON MICROSCOPY. (Jap.) Ota, Z. (Dept. Int. Med., Okayama U. Sch. Med., Japan), S. Suzuki and S. Higashi. Igaku To Seibutsugaku (Med. Biol.) 67(4):197-200, 1963.

An electron microscopic study was made of tissues in a 22-year-old Oriental male with meningitis due to leukemic infiltration and who had been treated with Myleran. Chloroleukemic cells obtained from the bone marrow contained inclusion bodies and intracytoplasmic virus-like particles which were round, were 100 mμ in diameter and 10 mμ in depth and were surrounded by a double membrane.

64-2155 TRANSMISSION OF KREBS ASCITIC MOUSE CARCINOMA 2 BY INOCULATION WITH CELL-FREE FRACTIONS. (Fr.) Thomas, J. A. (Lab. Cell. Biol., Sorbonne, Paris). *C.R. Acad. Sci.* 257(26): 4237-4240, 1963.

When cell-free fractions of Krebs Carcinoma 2 ascitic fluid were inj. i.p. into albino mice of various strains (wt. 25-30 g), fractions which contained RNA induced subsequently transmissible ascitic carcinoma in host animals. This ascitic carcinoma appeared to be both cytologically and cytochemically identical to that seen in animals inoc. with whole cells, and followed a comparable cycle of development.

64-2156 ULTRASTRUCTURE OF EXPERIMENTAL HEPATOMAS. (Fr., Abstract) Salomon, J.-C. and A.-M. Jézéquel. *Lyon Med.* 210(48):1145-1146, 1963.

Electron microscopic studies were not able to define any significant differences between the cells of malignant hepatomas and normal hepatocytes; nor was it possible to demonstrate the presence of viral particles in either spontaneously arising or experimentally induced hepatomas.

64-2157 AN ANALYSIS OF SV40-INDUCED TRANSFORMATION OF HAMSTER KIDNEY TISSUE IN VITRO. II. STUDIES OF THREE CLONES DERIVED FROM A CONTINUOUS LINE OF TRANSFORMED CELLS. (E.) Black, P. H. (Nat. Inst. Allergy Infect. Dis., Bethesda), W. P. Rowe and H. L. Cooper. *Proc. Nat. Acad. Sci. USA* 50(5):847-854, 1963.

Three clonal lines (2 epithelioid and 1 fibroblastic) were selected from hamster kidney cells transformed by SV40 virus (see CRA 1(8):#1548, 1963) in the presence of SV40 antiserum. No virus was detected in the supernatant culture fluids at any time and, with one exception, extracts of conc. cell suspensions containing 2-4 10⁶ cells/ml were free of detectable virus. Virus was recovered from all three clonal lines

by the overlay procedure, but, since the clonal line grew too fast and overgrew the monkey kidney cell indicator, blind passage was necessary for virus detection. Control monkey kidney cells never yielded SV40 virus. When 2-3 x 10⁶ cells of each clone at the 5th passage level were inoc. s.c. into 7 weanling hamsters, tiny s.c. nodules developed at the site of inoc. in all animals after 4-6 wk. and grew to a mean tumor diameter of 1 cm in the next 2-3 wk. The tumors grew much faster when the 3-3 clone was used than when the other two cell lines were used. SV40 virus was recovered from 2/5, 0/4 and 0/4 tumors derived from the 3-3, 4-1 and 4-2 lines, resp. Gross examination of the tumors showed that they resembled those arising from transplantation of the original transformed cell line; this was particularly true of tumors induced by 3-3. When the original cell line was studied for chromosome number prior to cloning, it was found that there was marked variability in chromosome number and morphology. In the 3 clones, during serial passages, there was a progressive alteration of the original stem-like karyotype (presumably that of the cell from which the clone derived). By the 35th passage clone 3-3 had a new modal number with a relatively low frequency of modal cells, clone 4-1 appeared to have become bimodal and clone 4-2 had a chromosome number distribution similar in shape to that of its earlier passages but with an entirely new modal number. The authors suggest that the SV40 genome is integrated in the genetic apparatus of a high proportion of transformed hamster kidney cells.

64-2158 TRANSMISSIBILITY OF BOVINE LEUKEMIA THROUGH ARTIFICIAL INSEMINATION. (Ger.) Rojahn, A. (Veterin. Inst., U. Gottingen, Germany) and A. Tolle. *Berlin. Munchen. Tieraerztl. Wschr.* 76(21):429-431, 1963.

The genetic transmissibility of leukemia was tested by hematologic studies on the offspring of two leukemic bulls (A and B) and one normal bull (C), used as donors of semen in artificial insemination. Hematologic examination of all the available offspring and mothers in 1961 showed that 6.7% of the offspring of A, 21.8% of the offspring of B and 11.7% of the offspring of C were leukemic; re-examination in 1963 revealed 6.1%, 3.9% and 5.6%, resp., were leukemic. At this time 4/5 leukemic offspring of A had leukemic mothers and 1/2 offspring of B. Of the leukemic offspring of C, 3/5 came from leukemia-positive stock. It was concluded that leukemia is not transmitted through the semen of bulls.

See also abstract nos.: 2052,2056,2058

64-2159 CARCINOMA OF THE COLON AND RECTUM IN GERIATRIC PATIENTS. AN ANALYSIS OF 300 CASES OF COLON AND RECTUM CARCINOMA IN RELATION TO AGE. (Flem.) Dequeker, J. (Dept. Int. Med., St. Rafeal U. Clin., Louvain, Belgium) and J. Vandenbroucke. T. Gastroent. 6(4):444-454, 1963.

The 1960 death rate for cancer of the stomach, colon and rectum in Belgium increased sharply and progressively for age groups between 45-65, plateaued for age group 65-75, then decreased as sharply as it rose. For the study group of 300 pts., cancers of the cecum and ascending colon were seen in 15%; of the transverse colon, in 9%; of the descending colon, in 6%; and of the sigmoid and rectum, in 66%. Carcinoma duplex was seen in only 3/300; and concurrent adenoma in 6.6%. Localization in the cecum and ascending colon was seen in 70% of the women pts. 70 yr. or older; in only 3% of the women pts. under 50. Sex distribution by age groups (all localizations) was: men--20-49, 36/62; 50-59, 45/75; 60-69, 53/106; 70 and older, 37/57; women--20-49, 26/62; 50-59, 30/75; 60-69, 53/106; 70 and older, 20/57.

64-2160 ETIOLOGY AND CLINICAL ASPECTS OF CIRRHOSIS-CANCER OF LIVER. (Rus.) Tareev, E. M. (Acad. Med. Sci. USSR, Moscow). Ter. Arkh. 35(8):19-26, 1963.

Among 231 pts. with primary cancer of the liver, 58.4% of all the cases showed cirrhosis-cancer of whom more than 26.7% showed evidence of "infectious hepatitis". The author believes that in at least one out of every 6 cases of primary liver cancer the cause is a virus infection. Average age at the time of death was 52 yr. for all 3 groups, i.e., cirrhosis-cancer and "infectious hepatitis" (i.h.), and "not infectious hepatitis" (n.i.h.) or cancer without cirrhosis (w.c.). Cirrhosis-cancer mostly affects males (83% in i.h., 87% in n.i.h., 72% in w.c.). The ratio between hepatoma:cholangioma was i.h. 3.6:1, and in n.i.h. 2.9:1; this relationship was not found in w.c. The duration of disease from the first clinical symptoms was less than 6 mo. in 60.8%, up to 1 yr. in 28.4% and more than 1 yr. in only 10.8% of the pts. Three case histories are reported in detail.

64-2161 SOME ASPECTS OF THE PATHOLOGY OF CARCINOMA PENIS. (E.) Reddy, D. J. (Dept. Path., Andhra Med. Coll., Vishakapatnam, India) and C. Indira. J. Indian Med. Assn. 41(6):277-280, 1963.

Among 580 cases of epithelioma registered at Guntur Medical College in the period 1954-1962, 163 were carcinoma of the penis; 156 of these occurred in Hindus, 7 in Christians and none in

Muslims. Incidence of carcinoma of the penis was highest in decades 4, 5 and 6 (34, 53, and 36 cases, resp.). Phimosis was seen in 20 cases. All of the pts. belonged to the low income group. Poor penile hygiene and noncircumcision among Hindus and Christians appear to promote the onset of carcinoma of the penis.

64-2162 CARCINOMA OF THE PENIS IN UGANDA AND KENYA AFRICANS. (E.) Dodge, O. G. (Dept. Path., Sheffield U., England) and C. A. Linsell. Cancer 16(10):1255-1263, 1963.

In Uganda carcinoma of the penis accounts for 12.2% of all cancer in males and 7.15% of all cases (including lymphomas and leukemia) recorded in the Kampala Cancer Registry. Peak of incidence occurs between yr. 45-54. In the county of Kyadondo, where a census was recently completed, the rate (per 100,000) is 3.76; the adjusted rate for the "standard African population" is 4.70. For comparison, the combined incidence of carcinoma of the penis and scrotum for Norway is 0.425. Circumcision depends more on religious than on tribal affiliation. It is practiced by African Moslems who, however, comprise only about 10% of the tribe in which they are most numerous (Ganda). At the Medical Research Laboratory, Nairobi, Kenya, 27 cases of penile carcinoma were seen in 1957-1961; this would represent 1.9% of all cancers in males and 1.0% of all cancer. In Kenya circumcision is practiced by most tribes; the exceptions include 2 tribes that account for the majority of cases seen in the territory.

64-2163 A STUDY OF EPIDEMIOLOGY OF STOMACH CANCER WITH SPECIAL REFERENCE TO THE EFFECT OF THE DIET FACTOR. (E.) Hirayama, T. (Dept. Epidemiol., Inst. Public Health, Tokyo). Bull. Inst. Public Health 12(2):85-96, 1963.

Death rates (per 100,000) due to stomach cancer in Japan for Japanese, Koreans, Caucasians and Chinese men, were, resp., 56, 54, 24 and 19; for women, 34, 17, 23 and 11. The rate for Japan is the highest in the world and appears to be still rising; however, the rate among Japanese in Hawaii and California has been declining in recent years. There is a greater association of stomach cancer in the lower socio-economic groups. There is marked regional variation with rates as high as 130; the disease is endemic in Hokuriku, S. Kanto and Kinki. Many dietary factors were investigated; there was no significant association with most factors; there was a slight positive correlation with excessive use of salty food and a negative correlation with deficient calcium intake. It is felt that the strategy of stomach cancer control in Japan should be directed toward changes in eating patterns of the Japanese, with special emphasis on promoting the drinking of milk and the reduction in consumption of salty foods.

- 64-2164 AN EPIDEMIOLOGICAL INVESTIGATION OF GASTRIC CANCER. (E.) Wynder, E. L. (Sloan-Kettering Inst. Cancer Res., New York), J. Kmet, N. Dungai and M. Segi. Cancer 16(11): 1461-1496, 1963.

A study of gastric cancer was made based on concurrent interviews of male and female, resp., gastric cancer pts. in: Japan (174 and 94); New York City (114 and 40); Iceland (48 and 9); Slovenia (31 and 20). In areas of high incidence of gastric cancer, common characteristics appear to be high intake of starchy foods (potatoes, rice and bread), with a concomitant low take of fresh fruits and vegetables. In some such areas there exists a relatively high use of home-smoked or charcoal-broiled foods. Results of the present study do not constitute evidence for or against a suspected relationship with vitamin A deficiency. Gastric cancer appears to occur more commonly in low socioeconomic groups; they tend to be more edentate (a finding most likely linked to nutritional deficiency). Among negative variables were tobacco and alcohol consumption, spices, rapidity of eating, mastication and temperature of food. Gastric ulcer plays a relatively minor, if any role, in the development of stomach cancer; however, achlorhydria, pernicious anemia and gastritis were not specially investigated in the present study. An extensive epidemiological review of clinical and experimental data is also presented (143 references).

- 4-2165 THE RELATION BETWEEN CONSUMPTION OF TOBACCO AND MORTALITY FROM MALIGNANT TUMORS OF THE LUNG, IN ITALY. (E.) Agnese, G. Translation of *Igiene Moderna* (Italy) 1958, v. 1(11/12), pp. 801-820. Cited in Tech. Transl. 0(9):1013, 1963.

On the basis of prospective and retrospective studies, there is a significant correlation ($P < 0.01$) between mortality due to lung cancer in 1953-1954 in the various regions of Italy and tobacco smoking in the preceding 25 yr. This increase was correlated with increase in cigarette smoking. Full translation available from SLA Translations Center (John Crerar Library, Chicago, Illinois 60616), number 63-16939, at a cost of \$2.60.

- 4-2166 PULMONARY TUMORS. (E.) Haintz, O. Translation of *Orvosi Hetilap* (Hungary) 1934, 78(30), pp. 684-687. Cited in Tech. Transl. 0(9):1017, 1963.

A study is presented of the increase in lung carcinoma, with analysis of various possible biological factors and relation to sex and age. Full translation available from SLA Translations Center (John Crerar Library, Chicago, Illinois 60616), number 63-16105, at a cost of \$1.60.

- 64-2167 AN EPIDEMIOLOGICAL INVESTIGATION OF CANCER OF THE BLADDER. (E.) Wynder, E. L. (Sloan-Kettering Inst. Cancer Res., New York), J. Onderdonk and N. Mantel. Cancer 16(11):1388-1407, 1963.

After a review of the literature (50 references) in which it is noted that information on bladder cancer is incomplete as to some areas of the world and as to occupation groups, a study by interview was made of 300 male and 70 female bladder pts. in several New York City hospitals; matched controls were selected from the hospital population excluding those with cancer of the lung, upper g.i. tract or with myocardial infarction. The disease is predominantly male and is increasing in some countries. A high correlation with cigarette smoking was confirmed, especially in those who smoke more than 20 per day. As to occupation, while the higher risk in aniline dye workers is well known, other occupations appear to have an increased risk, especially shoe repairers and leather workers. Also under suspicion are painting, hairdressing, certain textile operations, coal mining, and perhaps plumbing. There appears to be a positive association between bladder stones and bladder cancer. There are a variety of factors that do not seem to play roles in bladder cancer, including family history, alcohol consumption, intake of liquids, diet, and diseases other than bladder stones. Most excess cases of bladder cancer among males may be assumed to have exogenous causes.

- 64-2168 HEREDITY OF CANCER ELUCIDATED BY A STUDY OF UNSELECTED TWINS. (E.) Harvald, B. (Inst. Human Genet., U. Copenhagen, Denmark) and M. Hauge. J.A.M.A. 186(8):749-753, 1963.

In an unselected sample of 6893 Danish twin pairs a total of 1038 cases of cancer were found. Among 1528 probably identical twins the number of cancer probands with unaffected partners, partners with cancers of the same site, and partners with cancers of other sites were 143, 8, and 13, resp. The corresponding figures for 2609 fraternal twins of the same sex were 292, 9, and 39; for those of different sex 285, 5, and 34. The rate of concordance of cancer in general did not differ significantly between monozygous and dizygous twins, suggesting that development of cancer in general is not determined by genes, and that environmental factor(s) determine the diversity in the population with regard to cancer development. No discrepancies were found between the relative cancer mortality in the twin studies, and published vital statistics for Denmark.

- 64-2169 FACTORS IN THE FREQUENCY AND TYPES OF CANCER IN MAMMALS AND BIRDS AT THE PHILADELPHIA ZOO. (E.) Snyder, R. L. (Penrose Res. Lab., Zool. Soc. Philadelphia, Pa.) and

H. L. Ratcliffe. *Ann. N.Y. Acad. Sci.* 108(Art. 3):793-804, 1963.

Statistical analysis of cancer based on the records of the Philadelphia Zoo from 1901 through 1962 was possible for 9 families of mammals and 5 families of birds. The change after 1934 to a highly constant, high quality diet resulted in increased longevity with an accompanying increased frequency of cancer. Primary tumor sites appear to be randomly distributed. The frequency with which one or another site has been involved in one or more families may be interpreted, however, as suggesting the action of specific factors. Among these are familial relationships, dietary deficiency of iodine and thyroid cancer; a high frequency of carcinomas of the nasal mucosa in one exhibition group (*Procyonidae*); and an increase in lung cancers in ducks and geese. The overall frequency of cancer for animals exhibited longer than 12 mo. changed from 4% from 1901-1934 to 10.4% for the period 1935-1962. Frequencies of malignant tumors were generally lowest during the first quarter of life and highest in the fourth quarter. However, in most families the frequency of cancer was higher in each corresponding quarter during the period 1935-1962. Thus the increased frequency of malignant tumors was not merely a function of increased longevity. It is concluded that the level of susceptibility or the dosage of carcinogen rather than the duration of exposure to carcinogens has been the major determining factor (or factors if susceptibility and dosage both change) in increasing the frequency of cancer in these zoo animals.

64-2170 **EPIZOOTIOLOGY OF SPONTANEOUS CANCER IN CATTLE WITH PARTICULAR REFERENCE TO MALIGNANT LYMPHOMA.** (E.) Reisinger, R. C. (Agricul. Res. Serv., U.S. Dept. Agricul., Washington, D.C.). *Ann. N.Y. Acad. Sci.* 108(Art. 3):855-871, 1963.

The frequency of bovine malignant lymphoma shows a wide apparent variation within the U.S. (in 1960, from 3-95/100,000 in 13 different Meat Inspection Division stations in 7 states). Various marketing practices, economic factors and climatic conditions make it extremely difficult to relate incidence to factors associated with a particular area. There was a definite correlation with age: 90% occurred in cows over 5 yr. of age, 98% in cows 2 yr. old and older. Despite fluctuations in rate, it is believed that the frequency of carcass condemnations due to malignant lymphoma or other internal tumors has not increased from 1949 to the present time.

64-2171 **THE INCIDENCE OF MALIGNANT TUMOURS AMONG THE POPULATION OF THE RUSSIAN FEDERATION.** (E.) Kozlova, E. V. (P.A. Herzen Oncol. Res. Inst., Moscow). *Acta Un. Int. Cancr.* 19(5):877-881, 1963.

In 1961 the number of people (per 100,000) suffering from cancer in the Russian Federation av. 152.1. In an analysis of 155,424 reports (97% of all accounted cases) for 1960, the rate for all males was 121.1, all females 145.9. Cancer incidence among women up to age 50 was higher than for men; after 50 it was higher among men. When related to different large economic areas, the highest rate among men was found in the Volga region (140-150), and the lowest (up to 110) in both the W. Siberian region and the Central Black Earth (CBE) region. For cities, highest incidence for men was in the Volga region; for urban women highest incidence was in the Northwest and N. Caucasian regions, the lowest for both men and women was in the CBE region. For men frequency related to site (1st to 5th place) was: digestive tract; respiratory organs; mouth cavity and throat; skin; and urinary organs. Corresponding sequence for women was: digestive organs; the genitalia; skin; mammary gland; and respiratory organs. For both men and women highest incidence of cancer of the digestive tract was in the Northwest region; cancer of the respiratory and urinary organs and that of the thyroid gland were also highest in this region. For men highest incidence of oral cavity and throat cancer was in the N. Caucasus. The lowest incidence of these cancers for men was in the W. Siberian region (except oral cavity and throat, lowest in the Northwestern region, that of thyroid gland least in the CBE region). Regions of highest incidence for women for genital cancer was the Ural region and for mammary cancer in the Northwest and Central regions. For women areas of lowest incidence were: for digestive tract cancer, N. Caucasian region; genital cancer, the Central region; and mammary gland, the W. Siberian region. For both sexes skin cancers were highest in the N. Caucasian region and lowest for men in the Central region and for women in the Northwest region.

64-2172 **GUIDELINES FOR COOPERATION WITH DIRECTIVES CONCERNING AMBULATORY AND STATIONARY PUBLIC HEALTH PROGRAMS WITH A VIEW TO THE EARLY DETECTION, TREATMENT, AND POST-TREATMENT SUPERVISION OF CANCER PATIENTS IN THE GERMAN DEMOCRATIC REPUBLIC.** (Ger.) Wildner, G. P. (Inst. Publ. Health, Berlin-Lichtenberg). *Zschr. Aerztl. Fortbild. (Jena)* 57(21):1145-1147, 1963.

In a summary of East German laws governing the report, treatment, and post-treatment follow-up of cancer pts., the author reports that cancer deaths (per 100,000 of population) in 1961 were 219 as compared to 70 in 1900. Deaths due to cancer of the respiratory tract had risen from 9 for males and 4.4 for females, in 1932, to 62.5 and 7.9, resp., in 1960. The author cautions that the increase of deaths due to cancer in 1961, as compared to 1900, reflects improved diagnostic methods; increase of the av. male and female life spans, resp., from 42-66 and from 44-70 yr.; and a heavy weighting of the overall population in favor of older age groups, due to the heavy mortality in World War II.

4-2173 RESULTS OF THE MORBIDITY STATISTICS FROM CANCER IN THE GERMAN DEMOCRATIC REPUBLIC. (E.) Wildner, G. P. (Centl. Inst. Public Health, Berlin). Acta Un. Int. Cancr. 9(5):897-901, 1963.

From an analysis of 215,000 new cases of cancer (out of 400,000 reported) which occurred in the DR during the period 1953-1958, the effect of two World Wars is reflected in the greater crude rate among females. Age adjusted rate using the total population, however, indicates the greater cancer liability of males. The age adjusted rates (per 100,000) for all cancer in 1954, 1956 and 1958 was, resp.: for males--231, 254 and 266; for females--228, 241 and 255. Cancer in males is more frequent during infancy through puberty and again after yr. 55. The predominance of female cancer from yr. 15-55 reflects the frequent incidence of genital cancer. When genital cancer in both sexes is excluded, frequency in males predominates except between puberty and yr. 20-25 when it is about equal for both sexes. In males cancer of the lymphatic and hematogenic organs are most frequently involved until yr. 35, followed by the digestive system to age 85, and by skin cancer after 85. The lymphatic and hematogenic organs in females are also attacked most frequently in early yrs. but only to age 20 followed by genital organs from age 20-60, digestive organs to age 85 and finally by skin cancer beyond 85.

4-2174 MASS SURVEY FOR THE CANCER OF CERVIX UTERI IN CHINA. (E.) Kha-Ti Lim (Chinese Acad. Med. Sci., Peking), Kao Jun-Chuan and Chang Chih-Fen. Acta Un. Int. Cancr. 19(5):2-905, 1963.

On the basis of cervical smears, the prevalence rate (per 100,000, age adjusted) of cervical cancer in 4 areas of China was: Peking, 1,187 (7,787 examinations); Tientsin, 685 (44,453 examinations); Inner Mongolia, 887 (2,946 examinations); Shanghai, 699 (3,100 examinations). In 1693 cases, 78.2% were stage 0-1; highest incidence was between yr. 50-54. With age, the proportion of infiltrating tumors increases. Cervical erosion appeared to be a predisposing factor.

4-2175 ANTICANCER CAMPAIGN IN THE VINNITZA REGION. (Fr.) Danilenko, M. V. (16 Gogol St., Vinnitza, USSR), P. A. Chnevski and K. I. Berman. Acta Un. Int. Cancr. 19(5):895-896, 1963.

Distribution of cancers in the Vinnitza region (USSR) over the period 1956-1960 was uterus 19%, skin 18.5%, stomach 18.0%, lower lip 16%, lung 6.09%, breast 5.58%, esophagus 2.25% and other sites 30.32%. Cancer mortality fluctuates between 11.43-13.04%. Various aspects of integrated anticancer campaign involving

compulsory mass screening of women over 25 and men over 35 are discussed and some results are presented. The program is thought to be responsible for a reduction of undiagnosed cancers and for a decrease in cancer mortality from 81.2 to 61.3/100,000, with a corresponding increase in 3-year-cures.

64-2176 DISEASE AND DEATH IN CANADA'S NORTH. (E.) Willis, J. S. Med. Serv. J. Canada 19(9):747-768, 1963.

In a general discussion of the incidence of disease and the cause of death observed in Canada's Northwest territories, it is reported on the basis of provisional statistics that among an estimated population of 23,230 people (5,461 Indians; 8,282 Eskimos and 9,487 White Status) there were 10 deaths by neoplasm during the year 1962 with 7 occurring between the ages of 35-64 yrs. While these cases were verified by physicians, it is possible there might have been more among 12 deaths of unknown cause. While these numbers are small, the rates per 100,000 would be: Indians (2 cases) 37, Eskimos (5 cases) 61, and for White Status (3 cases) 32. The overall rate for Canada was reported as 8. In 1961, deaths from neoplasms for Indians, Eskimos and White Status were 19, 16 and 36. In 1962, 43% of all deaths were neonatal and infants under 1 yr.; 57% (including 1 death from neoplasm) were in children under 15 yr. of age.

64-2177 SALIVARY GLAND TUMORS IN CANADIAN ESKIMOS. (E.) Wallace, A. C. (Cancer Res. Lab., U. West. Ontario, London, Canada), J. T. MacDougall, J. A. Hildes and J. M. Lederman. Cancer 16(10):1338-1353, 1963.

Fourteen cases of salivary gland tumors in Canadian Eskimos are presented; 11 were malignant and only 3 were typical mixed tumors and 1 was an adenoid cystic carcinoma. The remaining 9 tumors were unusual in that they were poorly differentiated carcinomas that tended to invade locally and involve regional nodes. These cases were collected over a 9-year period and while exact incidence is not known, the number of carcinomas found in an Eskimo population of about 11,500 represents about 30 times that expected in a white population of similar size over the same number of years. Two cases were Inland Eskimos, the remainder lived on the sea coast. A consideration of the environment of the pts. gave no indication of possible etiology.

64-2178 LEUKAEMIA CLUSTERS. (E.) Milham, S. (New York State Dept. Health, Albany). Lancet 2:1122-1123, 1963.

An examination of death certificates of children under 10 yr. of age revealed that the overall incidence (per 100,000 population under 10 yr.)

in the 57 counties of upstate New York state was 4.3. In one county, Oneida, the incidence was 19.9 in 1950 and 14.9 in 1950-51. In Rome, a city in this county, the rate was 36.1 while in another city (Utica) the rate was 7.7 and in the remainder of Oneida County 12.0. In interviews carried out in September 1963 no common characteristics were discovered among the cases. The residences (1950) were not clustered and the cases or their sibs did not attend the same school. The mother of one of the cases died of acute leukemia at 28, a year after her son's death.

- 64-2179 SEASONAL VARIATION IN LEUKAEMIA INCIDENCE. (E.) Fraumeni, J. F. (NCI, Bethesda). *Brit. Med. J.* 2:1408-1409, 1963.

In a study based on data obtained by the National Cooperative Leukemia Survey of onset of leukemia in relation to season in children below the age of 16 during the yr. 1958-1961, it was found that a significant variation could be observed only in cases of acute lymphatic leukemia with relative increase in onset during the spring (March-May; 74/237 cases) and a relative decrease of onset during the summer months (June-August; 44/237). When all cell types were examined, it was found that there was a relative increase both during the winter (December-February; 135/511) and during the spring (143/511). The only group of acute leukemias which did not fall into this pattern was an acute type labeled "other and unspecified" (many were the stem cell type).

- 64-2180 CANCER AND DATE OF BIRTH. (E.) Davies, J. M. (Dept. Clin. Res., Roy. Marsden Hosp., London, S.W.3). *Brit. Med. J.* 2:1535, 1963.

After an examination of the month of birth of 2042 men dying of lung cancer in England and Wales during the yr. 1959 and 1960, the findings failed to confirm the higher incidence for February and March found by B. K. Dijkstra (CRA 1(9-10):#1772, 1964) in a series of 330 pts.

- 64-2181 LUNG CANCER AND MONTH OF BIRTH. (E.) Wal, A. M. v. d. (U. Hosp., Groningen, The Netherlands), H. J. Sluiter, K. de Vries and N. G. M. Orie. *Lancet* 1:114, 1964.

Data obtained from 150 pts. with lung cancer and 150 age, residence, and socioeconomic background-matched controls from The Netherlands failed to corroborate the findings of B. K. S. Dijkstra (see CRA 1(9-10):#1772, 1964). In the years 1888, 1895, 1899 and 1902, 25 lung cancer pts. were born; 22 were born in 1893, 1897, 1898, and 1900. No significant peak was noted among pts. born in March, and there were no significant differences in birth dates between the lung cancer group and controls.

- 64-2182 CIRCUMCISION AND CARCINOMA COLLI UTERI IN MACEDONIA, YUGOSLAVIA. RESULTS FROM A FIELD STUDY. II. COLPOSCOPICAL, CYTOLOGICAL AND HISTOLOGICAL FINDINGS. (E.) Stucin, M. (Gynec. U. Hosp., Ljubljana, Yugoslavia), S. Bon J. Kovačič, F. Hribar and L. Damjanovski. *Brit. J. Cancer* 17(3):400-405, 1963.

A systematic colposcopical and cytological study was attempted of 3633 women (1070 of them Moslem) in the Tetovo district of western Macedonia. Among 2555 non-Moslem women (94.6% of whom were examined), 145 out of 146 indicated biopsies were performed. Histological examination revealed 6 cases of carcinoma *in situ*, and 2 invasive cancers, as well as 17 instances of atypical epithelium. In a group of 540 Moslem women with sexual habits similar to those of non-Moslem women, on the basis of 26 biopsies, there was 1 carcinoma *in situ* and 1 invasive cancer and 1 atypical epithelium. Among 538 Moslem women following strict religious practices of sexual hygiene (including circumcision of males) while 18 biopsies were indicated, only 3 were performed. In this group there were no carcinomas and no atypical lesions.

- 64-2183 MORTALITY INDEXES FOR CHRONIC DISEASES AND MALIGNANT TUMORS. (Rus.) Shtraus, Z. E. (1st Moscow Inst. Med. (Order Lenin), USSR) *Vop. Onkol.* 9(12):22-26, 1963.

From the practical standpoint all pts. with malignant diseases die in 3 yr., yet the mortality index decreases. If, in 1957, there were 71.4% deaths (1,000/1,400), in 1959 there were only 56% (1,400/2,500). Mortality rate from all malignant neoplasms in Moscow was 32.8 in 1947, but only 25.9 in 1958. To compute the mortality rate properly the author suggests using the mean life span of treated pts. and not the mortality rate based on the total number of deaths within a given period of time, since this is confusing and provides insufficient statistics for the oncologist.

- 64-2184 BRONCHOPULMONARY CANCER AND ATMOSPHERIC POLLUTION. (Fr.) Fournier, P. *Rev. Tuberc. (Paris)* 27(78):853-855, 1963.

In a brief general review (no references), figures are presented on the incidence of cancer of the trachea and bronchi in France per 100,000 men. The rate rose from 14.3 in 1950 to 31 in 1961. The incidence was closely correlated to urban and industrial situations; this is shown in a map giving the incidence per 100,000 males (30 yr. or older) by departments. An increase of 1% in the non-agricultural population is correlated with 1 additional death/100,000 male inhabitants/yr. The role of smoking and industrial exposures is also discussed.

- 64-2185 EPIDEMIOLOGY OF CANCER IN BRAZIL. (Por.) Prudente, A. (A. C. Camargo Hosp., Sao Paulo Anticancer Assoc., Brazil). Rev. Brasil. Cir. 46(4):281-287, 1963.

In a preliminary assessment of racial and geographical considerations in relation to the incidence of different types of cancers, it is mentioned that too little information is as yet available concerning the pure Indian population living under primitive conditions. In the immigrant population, it was found that the incidence and localization of tumors follows pretty much the pattern seen in the countries of origin. In fact, a detailed study of Japanese immigrants shows that they are as prone to gastric cancer as Japanese living in Japan, and that the incidence is higher than that in any other group living in Brazil. Cancer of the esophagus appears to be more prevalent in the southern portion of the country, where the mortality rate (per 100,000 of population) was 15, compared with 4 in the large cities not located in that region. Deaths due to cancer of the esophagus in 1961 comprised 7.5% of all cancer deaths in the extreme southern city of Porto Alegre compared to 3.9% in São Paulo. In the former city, it was also found that 24.3% of all cancers in males were cancers of the esophagus. The author feels that in any study of these facts, the habit of ingesting very hot liquids must be taken into careful consideration. The incidence of penile cancer was found to be higher (11.4-24.6% of all cancers in males) in the northeastern part of the country (Bahia, Pernambuco and Alagoas) than in other sections of the country (1.7-3.9% of all cancer cases in males). The incidence of cancers of the cervix or the uterus were higher in the less-developed areas of the country. Tables of comparative values are given.

- 64-2186 SIGNIFICANT ASPECTS OF CHILDHOOD LYMPHOMA IN AFRICA. (E.) O'Connor, J. T. (NCI, Bethesda). Cancer Res. 23(9):514-518, 1963.

The outstanding clinical features and histopathological characteristics of malignant lymphoma in children in Africa are reviewed (13 references). Two features differ from lymphosarcoma elsewhere, and both have the same geographical distribution: an unusually high incidence (106 cases seen in Uganda in over 8 yr., 130 cases from Kenya in over 5 yr.) and a striking predilection for the jaws and face (presenting symptom in about 40% of cases). It is suggested that local environmental factors, such as endemic parasitic and virus diseases, rather than playing a direct etiologic role, may have an indirect effect, by altering host susceptibility and response. It is suggested that studies be extended to include systematic pathologic examination and comparative epidemiological studies of changes in the jaws and facial bones of children in the "lymphoma belt" and elsewhere,

with special attention to nonneoplastic changes affecting the lymphoreticular tissues.

- 64-2187 A LYMPHOMA SYNDROME IN TROPICAL AFRICA. WITH A NOTE ON HISTOLOGY, CYTOLOGY, AND HISTOCHEMISTRY. (E.) Burkitt, D. (Dept. Surg., Makerere U. Coll. Sch. Med., Kampala, Uganda) and D. H. Wright. Internat. Rev. Exp. Pathol. 2:67-138, 1963.

The clinical aspects of the syndrome are reviewed (68 references) with special reference to geographical incidence, age distribution, sex, tribal and racial incidence, tumor distribution, course and prognosis (see also CRA 1(3):#467, 1963). Studies by the junior author on histology, cytology and histochemistry are also reviewed. It is emphasized that a review of cases tend to support the conclusion that the poorly differentiated lymphocytic lymphomas of the syndrome show a uniform pattern, including as a characteristic feature large numbers of nonmalignant histiocytes with or without a clear or vacuolated form, and giving to sections a characteristic "starry sky" appearance. A section on epidemiological aspects brings together not only material from the literature but also results from inquiries and of personal investigations, especially in Africa. Finally there is considered evidence suggesting dependence of the lymphoma on external environmental factors, the probability of vector transmission and possible implication of a virus.

- 64-2188 AN IMPROVED MAP FOR THE STUDY OF BURKITT'S LYMPHOMA SYNDROME IN AFRICA. (E.) Haddow, A. J. (East African Virus Res. Inst., Entebbe, Uganda). E. Afr. Med. J. 40(9):429-432, 1963.

On the basis of more complete information on climatic conditions, parameters were redefined for the distribution of cases of Burkitt's lymphoma syndrome in Africa. The criteria used for excluding geographical areas were annual rainfall of 20 inches or under and/or areas where the mean temperature of the coolest month is 60°F or under. Only 7.5% of cases collected by Burkitt lie in the excluded area, and of these 4 (2.5%) are in the neighborhood of permanent swamps or lakes. (See also CRA 1(12):#2187, 1964.)

- 64-2189 CHARACTERISTICS OF WOMEN WITH VARIOUS GYNECOLOGIC CANCERS. (E.) Graham, J. B. (Roswell Park Mem. Inst., Buffalo, N. Y.). Obstet. Gynec. 23(2):176-181, 1964.

Consecutive records were reviewed for 100 each cancers of the uterine cervix, uterine body, ovary, vulva, breast, carcinoma *in situ* of the cervix, also for 50 cases of carcinoma of the uterine body and endocervix, and 41 of cancer of the vagina. The following parameters were examined: age, age at menarche and at menopause,

marital status and parity, height-weight relationships, glycosuria, and blood pressure. Four main groups could be distinguished. Cancer of the cervix occurred in a relatively young group, with about half premenopausal, only 10% sterile and no special proneness to glycosuria or obesity. The carcinoma *in situ* cases were remarkably similar to the frank cervical cancers but were younger by a decade, had even less sterility, and only about half as frequent hypertension. Similarities were also found between the pts. with cancer of the uterine corpus, and those with adenocarcinomas of the corpus and endocervix. Both groups had a peak in incidence at 60, had a high incidence of sterility, obesity, glycosuria, and hypertension. Vulva and vaginal cancer pts. showed a peak in the 70's, had a relatively high frequency of sterility, glycosuria and hypertension, but not of obesity. Some similarities were also observed between pts. with cancers of the breast and of the ovary, although those with ovarian cancer were younger, and less frequently obese or hypertensive than those with breast cancers. Sterility was present in about 1/3 in either group, and the frequency of glycosuria was low; in both, the age distribution curves showed 2 peaks.

- 64-2190 MORBIDITY STATISTICS. MALIGNANT NEOPLASMS IN CERTAIN COUNTRIES. (E. and Fr.) WHO (Geneve) 16(12):676-771, 1963.

This report deals with the analysis of malignant neoplasms in relation to site for certain countries over a period of years, where the information is available. This information is presented in some detail for Denmark, 1957-1959: the number of registered cases, morbidity rates and percentages according to site and sex. In addition, for the other countries, the number of registered cases and the percentage of cases at each site relative to total cases is presented by sex, all ages and by sex and age.

- 64-2191 SOME PROBLEMS OF THE ORGANIZATION OF ONCOLOGIC ACTIVITY IN THE MAROS-MAGYAR AUTONOMOUS DISTRICT. (Hun.) Kolumbán, M. (Marosvásárhely Med. Therap. Inst., Romania), J. Orbán, I. J. Farkas, Z. Ambrus and J. Kozma. *Orv. Szemle* 9(2):180-185, 1963.

For different regions of the district cancer morbidity and mortality are shown in graphs, according to site. Excluding the large "miscellaneous" category, gastric cancer was most frequent in 1962 (15.7%), followed by bronchopulmonary cancer (14.37%), skin cancer (11.70%), cancer of the uterus (9.20%), and cancer of the breast (5.20%). In the same year, mortality was greatest from gastric cancer (33.30%); cancer of the lungs accounted for 13.77% of the cancer deaths; cancer of the uterus (not including cervical cancer) for 6.40%; intestinal carcinoma (exclusive of rectal carcinoma) for 4.10%; leukemias

for 3.2%, and cancer of the breast for 3.14%. While the overall provincial cancer mortality was 17.18%, certain regions showed higher rates (up to 20.86% for Toplita). Prophylactic measures--general and specific--and the improvement of treatment facilities are discussed in the light of these findings.

- 64-2192 CANCER IN SAUDI ARABIA. (E.) Taylor, J. W. (Dhahran Health Ctr., Arabian Am. Oil Co., Saudi Arabia). *Cancer* 16(12):1530-1536, 1963.

A study of 193 male and 71 female pts. treated for cancer by Aramco facilities in Saudi Arabia during the 12-yr. period from 1950-61 indicated that lymphomas and leukemias (combined) constituted the type of neoplasm encountered most frequently (21.8% and 16.9%, resp.); while gastric cancers (18.7% and 14.2%, resp.) were the most common single type of tumor. Bronchopulmonary cancers accounted for 2.6% of the male cases (i.e., 5/193); with none reported in females. Among females the incidence of mammary and cervical cancers was 11.3% and 1.4%, resp. The author attributes the low incidence of bronchopulmonary cancers treated to the low incidence of smoking among Saudi Arabians; but attributes that of mammary and cervical cancers to the reluctance of Saudi women to be examined, and to their short life expectancy. However, he states that this reluctance for medical intervention of any kind extends to the entire "older generation"; and discusses at some length the possibility that the Saudi custom of packing the vagina with rock salt following delivery, the prevalence of male circumcision, and the virtual absence of promiscuity, may be partially responsible for the incidence of only 8 mammary and 1 cervical cancers among his total of 71 women treated in the course of 12 yr.

- 64-2193 CARCINOMA IN NEW ZEALAND AND COMPARISON WITH THAT IN ENGLAND. (Jap.) Segi, M. (Dept. Public Health., Tohoku U. Sch. Med., Japan) and Y. Narai. *Shindan To Chiryo (Diag. Treat.)* 51(8):137-140, 1963.

The incidence of carcinoma in 1958-1959 in New Zealand is presented according to site and sex and compared to that in England.

- 64-2194 THE INCIDENCE OF THYROID CANCER IN ENGLAND AND WALES. (E.) Campbell, H. (Welsh Nat. Sch. Med., Cardiff, England), W. R. S. Doll and J. Letchner. *Brit. Med. J.* 2:1370-1373, 1963.

In a summary of mortality statistics for thyroid cancers in England and Wales, 1940-59, the death rate was slightly and irregularly higher in females than in males under 30; but approx. double in females from age 30, on. Incidence (per million of population) for all ages in 1940-49 was 4.06 and

11.22, males and females, resp. In 1950-59, it was 4.41 and 11.36, resp., compared to 5.03 and 10.77, resp., in the USA (whites). U.S. mortality rates were substantially higher than British in age groups under 25; the difference was progressively less marked between ages 25-39, and then disappeared entirely. (However, the U.S. mortality rate in males continued to be higher than the British; the U.S. mortality rate in females, lower.) In England and Wales, mortality as a percentage of incidence was 4-5% under age 30; then increased progressively in 5-year-cohorts through 79 and 80+ from 8-85%. Between 1954-58, estimated total incidence in England and Wales, ages 0-14, 15-24 and by 5-year age groups thereafter through age 79 was 0.19, 3.0, 6.9, 7.0, 10.3, 13.2, 16.5, 22, 32, 38, 54, 61, 62, and 60 at age 80 and older.

64-2195 POST-CRICOID CARCINOMA: REGIONAL INCIDENCE IN ENGLAND AND WALES. (E.) Jacobs, A. (Inst. Path., Welsh Nat. Sch. Med., Cardiff, England). *Brit. Med. J.* 2:1373-1375, 1963.

In England and Wales, the regional incidence (per 1,000,000 of population) of deaths from post-cricoid carcinoma during 1957-61 ranged from 1.4-6.7 in the male population; but from 3.6-21.4 in the female population. The two highest regions of incidence (10.7 and 21.4 for females; 2.6 and 6.7, resp., for males) were in the two regions which comprised Wales. Three other regions, in England, showed a 2.6 rate for males; incidences in the same areas for females were 5.3, 5.4, and 8.0. The area of highest incidence for both men and women corresponded closely to that for gastric carcinoma; the area of lowest incidence was also one of the areas of lowest mortality rate for gastric neoplasms. A statistically significant relationship to the incidence rate of pernicious anemia was also demonstrable. Analysis of mortalities during 1959-61, in terms of social classes and of age groups from 35 upwards, showed no significant differences, except that no deaths among males 75 yr. and older were reported from the region comprising South and East Wales.

64-2196 CLINICAL AND PATHOLOGICAL OBSERVATIONS OF RENAL TUMORS. (Jap.) Fujii, Y. Hiroshima Citizens Hosp., Japan) and T. Shiraga. *Acta Urol. Jap.* 9(6):306-314, 1963.

Among 5,385 urological pts. observed during 8 yr., 11 renal tumors were confirmed by operation (200 nephrectomies) and 1 autopsy. The age range of the 11 pts. was 20-75 and 7 cases occurred between 40 and 60 yr.; 9 were males and 2 females. Four were exposed to the A-bomb at Hiroshima at varying distances (meters) from the hypocenter: 2 at 1,800, 1 at 2,000 and 1 at 5,000. However, the relation between this exposure and the appearance of the tumors is hard to assess.

64-2197 STUDIES OF DANIS' TEST AND INDICAN TEST IN GAS POISONING PATIENTS. (Jap.) Fujito, T. *Kyosai Iho (Med. J. Mutual Aid Assn.)* 12(1):155-156, 1963.

Some workers formerly engaged in the production of poison gas during World War II still had symptoms of cough and expectoration some 10 odd yr. later and there appeared to be a high incidence of malignancy in this group. Among 103 pts., 7 had cancers and the urine of 2 was positive for the Danis and indican tests. Repeated twice a yr., 6/7 became positive during the yr.

64-2198 KAHLER'S DISEASE IN THE AFRICAN. (REPORT OF 38 CASES.) (Fr.) Payet, M. (Med. Clin., Gen. Fac. Med. Pharm., U. Dakar, Senegal), M. Sankale, P. Pène and B. Diop. *Bull. Soc. Med. Afr. Noire Lang. Franc.* 8(3):338-343, 1963.

The first case of multiple myeloma in Dakar was reported in 1951, the second in 1953. At the time of publication, a total of 38 (28 males, 10 females) had been found, including one 12- and one 19-year-old, although the usual age of incidence was approx. 50. Race, ethnic group or religion did not appear to be an etiologic factor although no cases were observed among the Sereres or the Diolas. It was found primarily in rural areas. However, the authors consider the disease an illustration of predisposition toward disorders of the reticular and histiocytic systems on the part of black Africans.

64-2199 LEUKEMIA, MULTIPLE MYELOMA, AND APLASTIC ANEMIA IN AMERICAN RADIOLOGISTS. (E.) Lewis, E. B. (Div. Biol., California Inst. Tech., Pasadena). *Science* 142:1492-1494, 1963.

A survey of 425 death certificates of American radiologists dying between the ages of 35-74 during 1948-61 revealed a highly significant excess of deaths from leukemia, multiple myeloma, and aplastic anemia. Actual mortalities were 12, 5, and 4, resp., against normal expectancies of 4.02, 1.01, and 0.23, resp.; P values were 0.001, 0.004, and 0.0001, resp. (P was > 0.05 for lymphosarcoma, Hodgkin's disease, and lymphoblastoma). There were no deaths ascribed to chronic lymphatic leukemia, suggesting that radiation exposure (or some factor acting in a similar manner) was responsible for the mortality rates reported.

64-2200 ORGANIZATION OF CANCER SERVICE IN BYELORUSSIA. (Fr.) Alexandrov, N. N. (Res. Inst. Med. Oncol. Radiol., Minsk, USSR), T. T. Poddoubnaja and M. E. Zablotski. *Acta Un. Int. Cancr.* 19(5):882-884, 1963.

Following a general outline of the organization of clinics which in a single year examined 40-45%

of the population of the republic, it is reported that in 1961 0.06% of urban population was found to have malignant tumors while 1% had pretumoral conditions. In the rural areas these values were 0.17 and 0.65%, resp. The malignant tumor incidence per 100,000 population was 125.4 in the cities, 147.6 in the rural areas and 140.0 for the entire republic. When the incidence by sex was standardized for age, the incidence for men was higher (171.8) than for women (120.5). The incidence was found to increase with age; 92.9% of all pts. with cancer were more than 40 years old. At age 70 and over rates were 1069.6 for men and 547.4 for women; comparative figures for age 50-59 were 424.1 and 333.9, resp. Cancer of the uterus was most frequent in women in the age bracket 50-59 years. Lung cancer affected men ages 60-69 years; women of this age showed the highest incidence of mammary cancer. The rates (corrected for age) for men and women, resp., for selected sites were: stomach 76.7 and 44.4; epidermis 14.1 and 13.0; bronchi, lungs and pleura 22.2 and 5.6; lip 11.9 and 1.0. Cancer of the g.i. system affected 53.0% of men and 40.7% of women while 18.8% of the females had mammary cancer and 18.2% cancer of the uterus. Those affected (men, women) with cancer of the larynx were 2.1 and 0.2%; cancer of the lung, 13.8 and 3.6%, resp.

- 64-2201 EXPERIENCE IN THE OUT-PATIENT TREATMENT OF PATIENTS WITH PRECANCEROUS CONDITIONS. (Fr.) Nagimov, I. B. (Baturina St., Kazan, USSR) and N. M. Maikinson. Acta Un. Int. Cancr. 19(5):931-932, 1963.

Analysis of records shows that for every 100,000 of population, 419 cancer pts. and 1350 "precancerous" pts. are under periodic examination in Kazan. Although details are not given, the authors appear to classify as precancerous, pts. with gastric polyposis, mastopathy and some gynecologic lesions; there is a further subdivision of "precancerous" pts. into "facultative" (6384 pts.) and "obligatory" (410 pts.). It is stated that the cancer/precancerous pt. ratio in Kazan is 1:12 for gastric, 1:4 for uterus, and lower for breast. The male/female sex ratio is 39/61 among precancerous and 32/68 among cancer pts. As to age, 60% of the precancerous pts. were under 50, while 76% of the cancer pts. were over 50.

- 64-2202 BRONCHOPULMONARY CANCERS IN CHRONIC ARSENIC INTOXICATION AMONG WINEGROWERS IN BEAUJOLAIS. (Fr.) Galy, P., R. Touraine, J. Brune, P. Gallois, R. Roudier, R. Loire, P. Lheureux and T. Wiesendanger. Lyon Med. 210(43):735-744, 1963.

Four cases (1 female, 3 males; ages 51-62 yr.) are presented of winegrowers with pulmonary cancer and cutaneous hyperkeratosis due to exposure to arsenic. In 1 case the hyperkeratosis was present 20 yr. before diagnosis of cancer; in 2 cases

chronic bronchitis had been present since exposure to the arsenic (primarily 1940-1944).

- 64-2203 PULMONARY CANCER OF ARSENICAL ORIGIN AMONG WINEGROWERS IN BEAUJOLAIS. (Fr.) Galy, P., R. Touraine, J. Brune, P. Roudier and P. Gallois. J. Franc. Med. Chir. Thorac. 17(3):303-311, 1963.

See CRA 1(12):#2202, 1964.

- 64-2204 CIRCUMCISION AND THE INCIDENCE OF CARCINOMA OF THE PENIS AND THE CERVIX. A STUDY IN KENYA AND UGANDA AFRICANS. (E.) Dodge, O. G. (Dept. Path., Sheffield U., England) C. A. Linsell and J. N. P. Davies. E. Afr. Med. J. 40(9):440-444, 1963.

In a study of the incidence of carcinoma of the cervix, this cancer accounted for 9.4% of all malignancies in the Kampala registry in Uganda and 6.6% of those seen at the Medical Research Laboratory in Nairobi, Kenya. There appeared to be no correlation between circumcision of the males and the incidence of this type of tumor. For a discussion of carcinoma of the penis in these areas, see CRA 1(12):#2162, 1964.

- 64-2205 A COMPARATIVE STUDY OF THE FREQUENCY OF CARCINOMA OF THE STOMACH. (E.) Boles, R. S. (Philadelphia Gen. Hosp., Penna.), J. Ipsen, Jr. and J. Ruedy. Cancer 16(12):1584-1588, 1963.

A review of 675 cases of gastric carcinoma verified at autopsy at the Philadelphia General Hospital between 1867 and 1959 indicated a rate of incidence/100 autopsies of 1.93 in 1867-79, 2.20 in 1880-1919, 2.00 in 1920-29, and 2.02 in 1959. The rate of incidence for 1950-59 was not markedly different from that reported among all deaths in the State of Pennsylvania. Age-, sex-, and race-standardized tabulations showed a decline (1920-29 compared to 1950-59) among white men and among all women, but an increase of incidence among male negroes. A matter having an important bearing on interpretation of mortality statistics based on clinical diagnoses is the correctness of clinical diagnosis, which was increased from 54% in 1920-29 to 74% in 1950-59.

- 64-2206 BALANCE IN DISTRIBUTION OF MALIGNANT TUMORS. (Ger.) Mittmann, O. (Clin., House 12, Bonn-Venusberg, Germany). Krebsarzt 18(9/10):337-340, 1963.

In a study of mortality between 1933-61, recorded deaths from neoplasia among males over 1 yr. of age in Denmark increased from 15.1 to 22.4%; for females over 1 yr. of age increase was from 17.1 to 25.1%. Sex differences of incidence were not statistically significant. Between 1927-61, comparable tabulations for Norway were: males over

1 yr. of age, 11.4-18.1%; females over 1 yr. of age, 12.1-19.0%. While the increase of incidence was essentially a uniform trend for both sexes in Denmark throughout the period involved, the incidence among both sexes in Norway peaked in 1951-52 (males, 19.4%; females, 20.1%), with a gradual, slight decline thereafter. The author notes that changes in the incidence of a specific tumor type or types among males appear to be compensated by changes in the incidence of another type or types among females, in such a way as to maintain a relatively constant relationship in terms of overall incidence among the 2 groups, with somewhat more female than male cancer cases.

64-2207 CARDIOVASCULAR DISORDERS AND TUMORS IN RELATION TO THE TOTAL INCIDENCE OF ILLNESSES. (Sw.) Wijkström, S. *Svensk Lakartidn.* 50(45):3313-3325, 1963.

Among civilians who were hospitalized and studied completely in Sweden between 1946-1961 there were 2,005 with intrathoracic tumors (0.04%). Among 1.9 million of military personnel studied between 1950-1962, 113 had intrathoracic tumors (0.006%). Of the tumors in question, 58% were malignant, and 26% of these malignant tumors were metastatic. In contrast, the total incidence of intrathoracic tumors in Stockholm, in a comparable group (1949-1960), was 0.075%, of which 82% were malignant and 23% of these were metastatic.

64-2208 EPIZOOTIOLOGY OF LYMPHOSARCOMA IN CALIFORNIA CATTLE. (E.) Theilen, G. H. Dept. Med., U. California Sch. Veterin. Med., Davis), R. D. Appleman and H. G. Wixom. *Ann. N. Y. Acad. Sci.* 108(Art. 3):1203-1213, 1963.

Data derived through the first year's operation of a bovine lymphosarcoma registry in California confirmed the existence of the disorder in 88 cows and 2 steers: 79 dairy cattle (70 Holstein-Friesians, 3 Guernseys, 3 Jerseys, 2 Milking Shorthorns, 1 Ayreshire); 8 beef cattle (5 Herefords, 1 Angus, 2 cross-breeds); and 3 animals without record as to breed. Estimated incidence (per 100,000 cattle), by age-groups (yr.), was: 0-2, <1; 2-3, 1; 3-4, 1; 4-5, 1; 5-6, 9; 6-7, 22; 7-8, 34; 8-9, 24; 9-10, 0; 10-11, 15; 11-18, 55. The overall estimated incidence/100,000 adult dairy cows was 8; for adult beef cows, 0.58. Among 74 dairy cows which could be traced to 66 ranches of origin, 45 had been raised on the ranches involved; 18 of these came from 10 multiple-incidence herds with a total population of 866 animals and a 1961 lymphosarcoma rate of 20 (in contrast to an incidence rate of 300 in 3 single-incidence herds with a known population of 9,185 animals). Of 10 multiple incidence herds, 2 were purebreds: Milking Shorthorn and Holstein-Friesian. The 8 other herds were grade Holstein-Friesian cattle. Six of the herds were in the Sacramento Valley, 3 in the San Joaquin Valley, and 1 in southern California. The high

incidence reported for the Sacramento Valley could, according to the authors, be due to the proximity to the investigating team. However, it is mentioned that personal inquiries of practicing veterinarians and slaughter house inspectors have revealed that the disease is actually rare in the northern part of the state and in the coastal area north of the Sacramento Valley.

64-2209 PEDIGREE STUDIES IN BOVINE LYMPHOSARCOMA. (E.) Croshaw, J. E., Jr. (U. Pennsylvania Sch. Veterin. Med., Philadelphia), D. A. Abt, R. R. Marshak, W. C. D. Hare, J. Switzer, J. Ipsen and R. M. Dutcher. *Ann. N. Y. Acad. Sci.* 108(Art. 3): 1193-1202, 1963.

In nearly all of 14 multiple-case lymphosarcoma herds there were statistically significant aggregations of lymphosarcoma cases. Both sire or cow family aggregations could show important aggregations. The authors feel that such group aggregations are compatible with a concept of genetic susceptibility to lymphosarcoma and/or vertical transmission of an agent as yet unidentified.

64-2210 CARCINOMA OF THE ENDOMETRIUM. (E.) Hoge, R. H. (1200 E. Broad St., Richmond, Va.). *Virginia Med. Monthly* 91(1):10-14, 1963.

A review of the incidence, diagnosis and treatment of endometrial carcinoma suggests that the overall incidence is increasing, both absolutely and in relation to the incidence of cervical carcinoma, with a peak incidence occurring approx. 10 yr. later than that of cervical carcinoma. The phenomenon may be related, at least in part, to increasing longevity. The author feels that unopposed estrogen stimulation may be a major etiologic factor, and says that progestogens exert a palliative, and possibly, a prophylactic effect. Incidence is higher in the higher social and economic groups. In New York city, in 1952, incidence was 15.2/100,000 Jewish females, 12.6 for other whites, 7.8 for Puerto Ricans, and 9.2 for Negroes. Comparable tabulations of incidence for cervical carcinoma were 3.6, 13.5, 97.6, and 47.8, resp. The ratios of cervical to endometrial carcinomas, were, resp., 0.23, 1.07, 12.5, and 5.19. In Puerto Rico itself, this ratio is 1:14.

64-2211 LUNG CANCER AND MONTH OF BIRTH. (E.) Baas, C. (U. Cancer Registration Ctr., Wilhelmina Gasthuis, Amsterdam, The Netherlands) and J. Strackee. *Lancet* 1:47, 1964.

A statistical analysis of 1346 cases of lung cancer in the western part of The Netherlands failed to yield any significant correlation between susceptibility to this disorder and the month of birth.

64-2212 AIR POLLUTION AND ITS HEALTH EFFECTS IN JAPAN. (E.) Toyama, T. (Dept. Preventive

Med., Keio U. Sch. Med., Tokyo). Arch. Environ. Health (Chicago) 8(1):153-173, 1964.

For 1960-1961 the av. monthly dustfall (by deposit gauges) ranged from 11-39 tons/km²/mo.; SO₂ conc. (by PbO₂ cylinders) ranged from 0.3 to 1.8 ppm in the Japanese cities where air pollution is a community health problem. In the factory area of Kawasaki, peak dustfall is in the spring and often reaches 70 tons/km²/mo. Between 1956 and 1959, the correlation coefficient between monthly dust fall and deaths due to lung cancer in 21 districts of Tokyo (42 samples) was not significant (0.109); that for bronchitis was highly significant (0.407, $P = < 0.0005$). For 1961, the proportional morbidity ratio (per cent) for malignant tumors in heavily industrial Kawasaki was 0.4; for an urban and industrial section of Yokohama 1.5; for a suburban, residential area of Kainan 0.6; and for rural Daito village, 2.8. The age standardized morbidity rates (per 1,000) for malignant tumors in Kawasaki, Yokohama, and Daito were, resp., 0.6, 1.2, and 1.6.

64-2213 TOPOGRAPHIC DISTRIBUTION OF CANCERS OF THE LARYNX AND PHARYNX IN SYRIA. (Fr.) Chahine, Mouradi, Osman and M. S. Amini. Ann. Otolaryng. (Paris) 80(12):943-946, 1963.

Laryngeal cancers are less frequent in Syria than in Europe or America, although their relative frequency among Syrian women is higher. They are found almost exclusively in cigarette smokers, with only 2 cases recorded among nonsmokers and only 1 among smokers who use a water pipe exclusively. They are only very rarely metastatic, and occur without demonstrable adenopathy in 75% of the cases. Incidence in Damascus is 2/100,000 males and 0.4/100,000 females; while the rate for pharyngeal cancers is 0.5 and 0.4, resp. Included is a detailed analysis of sites of occurrence and histologic types, for both disorders.

64-2214 LEUKEMIC NEOPLASIA IN THE DOG. (E.) Smith, H. A. (Armed Forces Inst. Path., Washington, D. C.). Ann. N. Y. Acad. Sci. 108(Art. 3):633-641, 1963.

For diagnostic purposes, 301 cases of canine neoplasms filed at the Armed Forces Institute of Pathology during the last 25 yr. were viewed as belonging to a Lymphoma group (186), a Myelocytic group (28), a group with Hodgkin's-like lesions (7), a Mast-cell group (about 20), and a canine transmissible venereal tumor group (15). As regards lymphomas the disease is usually, but not invariably associated with advancing yr. Sex, breed, and month when first diagnosed appear to have no significance. The series did not lend

itself to an analysis by regions. In the lymphoma group, the organs involved were: lymph nodes (general) 148, tonsils 14, thymus (none), spleen 91, liver 72, kidneys 34, lungs 21, intestine 23, stomach 5, pancreas 10, heart 6, uterus 4 in 70 females, prostate 1 in 92 males, bladder 3, other sites 11. As to type, the classification was: 58 stem cell, 73 histiocytic, 21 lymphocytic, 19 poorly differentiated lymphocytic, and 15 mixed or unclassifiable. Of 16/28 with myelomatous neoplasia, 3 were of myeloid or granulocytic leukemia, while in 2 cases leukemia was definitely absent, in 11 information on this point was unavailable. In those with Hodgkin's-like lesions multinucleated giant cells, or cells with multilobed nuclei were present in all cases; many resembled the Reed-Sternberg cell. In reference to the group as a whole, all of the tumor types discussed were said to appear to arise from cells which, in the normal body, play an active and important part in reactions to irritants (inflammations). Since it is known that tumors of these kinds often yield some of their virulence to the same corticosteroid treatments that inhibit inflammation, the hypothesis is advanced whether these kinds of neoplasms may represent an excessive and abnormal stimulation of reactive processes against an irritant or combination of irritants which we may recognize in some other form.

64-2215 CANCER OF THE PENIS. A TENTATIVE SURVEY OF THE PROBLEM ON A NATIONAL SCALE. (Sp.) Woolrich, J. Rev. Confed. Med. Panam. 10(4):191-202, 1963.

In a general review (31 references), the author reports that, in Mexico, 45% of all pts. treated for cancers of the penis came from rural areas, 19.5% were servants, 16% were day laborers, approx. 7% were tradesmen and 7% were office workers; only a few, isolated cases were found among professional men and artisans. The incidence by age groups (by decades) was 0.47, 9.43, 16.51, 8.02, 22.17, 18.87, 16.51, 6.13, 1.89, and 0.00%. Comparable tabulations for cancers of the prostate were 0.33, 4.77, 4.93, 1.48, 6.74, 21.38, 30.60, 25.66, 3.78, and 0.33%; for testicular cancers: 3.85, 6.41, 30.77, 42.95, 8.97, 3.21, 1.28, 1.92, 0.64, and 0.00%. The incidence of renal cancers peaked abruptly at 41-50 yr. (21.57%) and 51-60 (26.14%), then dropped equally abruptly to its immediately preceding level of approx. 14%; while that of cancers of the bladder peaked more gradually: rising from 15.75% at 41-50 to 37.28% (51-60) and 29.66% (61-70), before dropping off to 9.19% for the decade following. In general, 11.98% of all male cancers of the genitourinary tract were cancers of the penis: an elevated incidence which the author ascribes to lack of personal hygiene and the fact that circumcision of newborn males is not a routine practice in many parts of Mexico.

See also abstract nos.: 2060, 2062, 2120

MISCELLANEOUS

64-2216 CARCINOMA IN PSORIASIS VULGARIS-- POST HOC OR PROPTER HOC? (Ger.)

Unna, P. J. (Clin. Derm., U. Hamburg, Germany),
A. Memmesheimer, Jr. and J. J. Herzberg. Arch.
Klin. Exp. Dermatol. 217(3):321-339, 1963.

Four cases are presented of carcinoma in pts. with psoriasis; all had been treated with arsenic or tar-containing drugs or X-ray at one time or another. One developed metastatic squamous epithelium carcinoma (SEC), precancerosis and hyperkeratosis; 1/4 developed multiple SEC, prickly cell carcinoma (PCC) and arsenic keratosis; 1/4 developed PCC, basaloma and histiocytoma; 1/4 developed a melanoma of the scrotum and a papillary acanthoma of the armpit. Besides 46 such cases already reviewed in the literature, data on 61 additional cases of psoriasis with carcinoma are presented in tabular form. The reports show that exogenous factors such as arsenic, X-ray and tar are almost exclusively responsible for carcinogenesis in psoriasis (72.3% of all pts. reported to date had a history of exposure to arsenic). Generally, cancer in psoriasis is an arsenic-induced cancer, never a psoriasis-induced neoplasm.

64-2217 LEUKEMIA IN BURKITT'S LYMPHOMA. (E.)

Clift, R. A. (Delta Clin., Port
Harcourt, Nigeria), D. H. Wright and P. Clifford. Blood 22(3):243-251, 1963.

Four cases are presented (1 Arab, 3 African boys) of Burkitt's tumor with terminal lymphoblastic leukemia which confirms the lymphomatous nature of the disease. While these findings might lend support to Dalldorf's speculation that the Burkitt tumor is an unusual manifestation of acute lymphoblastic leukemia of childhood, this hypothesis does not take into account the low incidence of both Burkitt's tumor and acute lymphoblastic leukemia in the highland regions of E. Africa and also S. Africa.

64-2218 TRAUMA AND SEMINOMA. (Ger.) Jantschew, W.

(First Med. Clin., Med. Res. Inst.,
Sofia, Bulgaria), N. Nedkow, E. Jordanow and
T. Natschew. Zschr. Ges. Inn. Med. 18(15):
709-712, 1963.

Among 53 cases of tumors of the testis in men aged 28-64 observed between 1950 and 1960, 46 were seminomas. In 8/46 (17.4%), the histologically verified seminoma had developed in 10 days to 7 mo. after injury to the testes.

64-2219 MALIGNANCY IN SCARS, CHRONIC ULCERS, AND SINUSES. (E.) Cruickshank, A. H.

Dept. Path., U. Liverpool, England), E. M.
McConnell and D. G. Miller. J. Clin. Path.
6(6):573-580, 1963.

Included among 44 cases of malignancies in scars, chronic ulcers, and sinuses are the following predisposing lesions: a 20-year-old sinus from ischial bursitis, a 23-year-old bed sore, a congenital syphilitic gumma about 50 yr. old, 3 burn scars (av. age of scar 56 yr.), 11 sinuses from chronic osteomyelitis, and 27 chronic leg ulcers (3 Wasserman reaction positive). Among the osteomyelitis cases were 2 rapidly fatal sarcomas, one in a sinus present for 16 yr., the other in a 20-year-old sinus; the remaining cases in this group were squamous carcinomas that developed in sinuses that had been present for an av. of 37 yr. In the cases of varicose ulcer, the ulcer had been present an av. of 21 yr. before onset of malignancy. One pt. in this group, with an ulcer apparently present for less than 5 yr., developed a sarcoma that was fatal in 6 mo. The conditions discussed are now known as "Marjolin's ulcer". In the series presented, the degree of malignancy appeared to be low in tumors arising in scars but high in those arising in chronic ulcers and sinuses.

64-2220 SQUAMOUS CELL CARCINOMA AT THE BASE OF AN X-IRRADIATED LUPUS VULGARIS.

(Ger., Abstract) Hoffman, R. Derm. Wschr.
148(31):134, 1963.

A case is reported of a 77-year-old woman who had a squamous cell carcinoma removed from the elbow, an area in which an inflammatory condition 25-39 yr. previously had been treated with irradiation (total 13,150 r). Remnants of lupus infiltrates were visible on the upper arm above the tumor site.

64-2221 VARIATIONS IN THE METASTATIC RATE OF BROWN-PEARCE TUMORS. (Ger.) Matthies, E.

(Pharmacol. Inst., Martin Luther U., Halle/Salle,
Germany) and J. E. Peters. Naturwissenschaften
50(15):526-527, 1963.

The incidence of metastases of a Brown-Pearce tumor maintained in rabbits in the authors' laboratory by site for 7 successive yr. was as follows (metastases/number inj.): kidney--14/27, 1/21, 0/45, 0/48, 6/38, 6/39, 1/14; lymph nodes--8/27, 0/21, 0/45, 0/48, 5/38, 4/39, 1/14; liver--5/27, 0/21, 0/45, 0/48, 1/38, 1/39, 0/14; lung--4/27, 0/21, 0/45, 0/48, 0/38, 1/39, 0/14; g.i. tract--3/27, 0/21, 0/45, 0/48, 1/38, 0/39, 0/14; skin--1/27, none during the remaining 6 yr. Total incidence of metastases (%) was: 59.3, 4.8, 0, 0, 18.4, 15.4, 7.1. There was no statistically significant relationship between the time of incidence of the first demonstrable metastasis (3.8-5.0 mo.) and the number of metastases observed.

64-2222 SOME ABERRATIONS IN METABOLIC PATTERNS OF MALIGNANT CELLS. (E.) Kalckar, H. M.

(Biochem. Res. Dept., Massachusetts Gen. Hosp., Boston) and E. A. Robinson. Biochem. Zschr. 338:763-770, 1963.

In a general discussion of galactose metabolism in malignant or potentially malignant cells, it is mentioned that the inhibition of galactose metabolism which has been observed in HeLa cells is probably not due to a lack of epimerase but rather to an inhibition of its activity by the accumulation of reduced DPN resulting from aerobic metabolism. Comparative transferase and epimerase values are given for normal mouse lactating mammary gland cells, Ehrlich ascites tumor (mouse), mammary carcinoma (rat), and HeLa cells. These data indicate that both activities are much decreased in all the tumor lines.

64-2223 EXPERIMENTAL STUDIES OF FACTORS INFLUENCING HEPATIC METASTASES. XIV. EFFECT OF PROLACTIN. (E.) Fisher, E. R. (Dept. Path., U. Pittsburg, Pa.) and B. Fisher. Cancer Res. 23(9):1532-1538, 1963.

After intraportal inj. of Walker tumor cells into hypophysectomized (hypox.) female Sprague-Dawley rats, i.p. admin. of ovine prolactin increased incidence and size of hepatic metastases. Such treatment in intact females increased the size but did not alter incidence of tumors while no effect was seen in intact or hypox. males. Prolactin elicited ductal and end-bud mammary growth only in hypox. females and additionally lobulo-alveolar proliferation in intact females and to a moderate degree in intact males. Other tropic effects were not seen in either sex. In contrast to previous experience, fresh pituitary extracts of the rat, beef, sheep and humans failed to influence tumor growth in hypox. female rats. These preparations exhibited somatotrophic, variable gonadotropic but no mammogenic activities.

64-2224 PARASITES AND CANCER: SARCOMA IN DOGS ASSOCIATED WITH SPIROCERCA LUPI. (E.) Bailey, W. S. (Dept. Path., Auburn U. Sch. Veterin. Med., Ala.). Ann. N.Y. Acad. Sci. 108(Art. 3):890-923, 1963.

During the period 1951 through 1962 necropsies revealed 32 dogs with sarcoma of the esophagus and 1 of the aorta; in addition 6 specimens of sarcoma of the esophagus were submitted by other veterinarians. There was direct or very strong presumptive evidence of existing or prior infection with S. lupi in 38/39 dogs. As to breed, this association was found in 24 hounds, 6 pointers, 6 setters, 2 mixed and 1 German shepherd. Association of sarcoma with Spirocerca appears to have been more prevalent during the last decade than previously; it now appears to be more common in the southeastern U. S. than elsewhere in the world. The striking association indicates a casual relationship.

64-2225 GENETIC ASPECTS OF CANCER WITH SPECIAL REFERENCE TO CANCER OF THE EYE IN THE BOVINE. (E.) Anderson, D. E. (Dept. Biol., U. Texas M. D. Anderson Hosp., Houston). Ann. N.Y. Acad. Sci. 108(Art. 3):948-962, 1963.

In an investigation of bovine ocular squamous carcinoma in 3,334 animals of 25 breeds and breed crosses, it was found that the breed groups differed in susceptibility and that this susceptibility was related to the degree of pigmentation of the bulbar conjunctiva (as measured directly by recording color in 60 squares of a plastic overlay). This pigment was also shown to have significant inhibitory or protective effect against lesion development in individual animals. A genetic basis was found to exist for this pigment and for susceptibility of the conjunctiva. It was concluded that genes apparently determine susceptibility of the eye indirectly by determining the degree of pigmentation.

64-2226 RECENT ACQUISITIONS IN MALIGNANT TRANSFORMATION OF ANIMAL CELLS IN VITRO. (E.) Barski, G. (Gustave-Roussy Inst., Villejuif, Seine, France). Folia Biol. (Praha) 9(5): 323-328, 1963.

A general discussion and review (26 references) is presented of the possible mechanisms which are involved in the phenotypic expression of genetic traits for malignancy acquired in vitro by cells derived from normal tissues. The author in collaboration with R. Cassingena explanted adult lung tissue of a C57BL female mouse; the culture was divided into 2 culture groups. One group was transferred by trypsinization (PT line), the other only by mechanical dispersion (PG line). The PT line starting from mo. 6 of culture produced tumors in isologous mice while PG, after 18 mo. in vitro was still unable to give rise to tumors. While both cultures were of a general connective tissue-like appearance, the PT cells had a much more pronounced fibroblastic aspect with more tendency to form a dense intermingled tridimensional network. The morphological differences were not altered by changing treatment: mechanically dispersing the PT lines or trypsinization of the PG line. However this trial must be extended in time. Many changes (hypotetraploid karyotypes after 142 days, increase in abnormal metacentric chromosomes after 9 mo.) occurred in both lines. However, these changes were accompanied by the acquisition of malignancy in one case (PT) and not in the other (PG).

64-2227 OBSERVATIONS ON THE TUMORAL TRANSFORMATION OF TOBACCO TISSUES CULTURED IN VITRO. (Fr.) Duarte, I., G. Spangersberg and R. Gautheret. C.R. Acad. Sci. 257(19): 2782-2785, 1963.

When tobacco stem cultures which had been cultured

in vitro in the presence of both auxin (indolyl-acetic acid 3×10^{-7} or 2,4-dichlorophenoxyacetic acid 10^{-7} , units not stated) and kinetin were grafted in contact with the cambium of young tobacco stems, there was only 1 take in 38 grafts, with the formation of an abortive tumor. When the graft material used consisted of cultures which had been grown in the presence of auxins alone voluminous tumors were formed in 14/21 grafts. The remainder rapidly necrosed, possibly due to poor nutrition. The cultures in the presence of both auxins and kinetin grew exuberantly while in the presence of auxins alone they degenerated after a few passages. When cells from the former cultures were transferred to medium devoid of both auxins and kinetin growth stopped immediately and degeneration followed within 1 mo. The authors feel that the tumorigenic action of auxins is not due to the compounds themselves but rather to a disequilibrium (hormonal).

64-2228 MELANOMA IN AN ALBINO. (E.) Kennedy, B. J. (Dept. Int. Med., U. Minnesota Med. Ctr., Minneapolis) and A. S. Zelickson. *J.A.M.A.* 186(9):839-841, 1963.

A 38-year-old pure albino male developed and died of metastatic melanoma which apparently originated in a pink nodule present on the left thigh since birth. Electronmicroscopic study of the melanoma showed that the tumor was composed of pigment forming cells. Within many of the tumor cells it was possible to show premelanosomes and melanosomes. The nuclei of the tumor cells were large, irregular in contour and limited by a double membrane. The cytoplasm was filled with organelles but appeared clear because of a decreased number of ribosomes. Mitochondria were abundant and on the whole morphologically typical. Centrioles and mitotic figures were often present and closely associated with Golgi complex. The Golgi apparatus consisted of many vesicles which were vacuolated and swollen. The melanosomes, which were associated with this complex, were found to oval, limited by a smooth-walled membrane and ranged from 0.2 to 0.5 μ in size. The endoplasmic reticulum was also hypertrophied. There were no mature melanin granules.

64-2229 CYTOGENETIC STUDIES IN CHILDREN WITH ACUTE LEUKEMIA. (E., Abstract) Towns, D. (U. Louisville Sch. Med., Ky.). *Southern Med. J.* 56(12):1447-1448, 1963.

In seven children in whom the usual mode of treatment was unsuccessful or in whom the usual therapeutic agents had lost their efficacy, other treatment (not specified, but not employing cytotoxic agents), in addition to being clinically beneficial resulted in cell cultures which yielded numerous metaphases. Aneuploidy was observed in approx. 65% of the cells studied with a range of from 27-54 chromosomes; polyploidy was noted in about 2% of the cells. The author states that

since the agents used to treat these pts. had been shown not to affect adversely the growth of cells in tissue cultures, the aneuploidy which is observed in acute leukemia of childhood is truly a manifestation of the disease and not an effect of treatment.

64-2230 CYTOGENETIC STUDIES IN BURKITT'S LYMPHOMA. (E.) Jacobs, P. A. (Western Gen. Hosp., Edinburgh, Scotland), I. M. Tough and D. H. Wright. *Lancet* 2:1144-1146, 1963.

Chromosome preparations of the peripheral blood of 9 pts. with Burkitt's lymphoma and the bone marrow preparations of 8 of the cases were indistinguishable from normal. Upon examination of tumor preparations of 10 pts. who were untreated, cytogenetic changes were seen in 6 (4 of the preparations were judged "inadequate"). Since 4 of them showed no abnormalities, if the biopsy was representative of the tumor, then a proportion of these tumors are not associated with observable changes. Adequate tumor preparations of 3 cases previously treated with cyclophosphamide were all abnormal, though it is impossible to say whether or not these abnormalities arose as a result of treatment. Among 9 pts. with chromosome abnormalities 5 (4 untreated) had in all or in the majority of the cells of the tumor an abnormal large acrocentric chromosome the size of the long arms of a no. 2; in 4/5 the cells involved lacked a chromosome no. 2. Further studies are required to determine whether these chromosomes are affected with a frequency greater than normal, and if so, whether this is of any significance to the suggested viral etiology of Burkitt's lymphoma.

64-2231 A CASE OF DOWN'S SYNDROME WITH THE PHILADELPHIA CHROMOSOME, CHRONIC MYELOGENOUS LEUKEMIA, AND LOW LEUKOCYTE ALKALINE PHOSPHATASE. (E., Abstract) Cawein, M. J. (Dept. Med., U. Kentucky Coll. Med., Lexington) and E. J. Lappat. *Clin. Res.* 12(1):32, 1964.

A case is reported of a 45-year-old woman showing Langdon Down's syndrome, with chronic myelogenous leukemia, an acrocentric chromosome belonging to the 21-22 G group and low leukocyte alkaline phosphatase. The case is considered to be the first reported in the literature which presents this combination.

64-2232 A COMPARATIVE STUDY OF BASAL CELL AND SQUAMOUS CELL CARCINOMA IN DOGS AND MAN. (Ger.) Bosse, K. (Dermatol. Clin., U. Munich, Germany) and E. Weiss. *Berlin. Munchen. Tierärztl. Wschr.* 76(19):387-390, 1963.

In a general review of the sites of incidence, course, treatment, and prognosis of human basal cell and squamous cell carcinoma of the skin, the authors conclude that a close parallelism exists between man and dogs, as concerns the most frequent

sites of incidence. In dogs, there also appeared to be a significant correlation between the sites of incidence of 75 cases of squamous cell carcinoma (21% on the back; 31% on the extremities) and 100 cases of bite wound in noncancerous animals (27-28% on the back; 30-31% on the extremities). In one animal, a squamous epithelial cell carcinoma appeared on the site of an old bite scar (7 references).

- 64-2233 CONSIDERATIONS ON THREE CASES OF VERRUCIFORM EPIDERMODYSPLASIA OF LUTZ LEWANDOWSKY. (Por.) Campos, S. (Derm. Clin. U. Recife, Pernambuco, Brazil), F. Maciel, J. Lôbo Filho, M. Lôbo Jardim and W. Bandeira. An. Brasil. Derm. 37(1-4):19-34, 1962.

Two brothers (ages 34 and 14 yr.) developed disseminated, slightly raised papulous lesions early in life and later ulcerating lesions. The latter were diagnosed as epidermoid cancers. The older brother died of cancer in spite of electrocoagulation and radium therapy, while the younger was discharged cured. A third case (a 31-year-old man), whose maternal and paternal grandparents as well as parents were first cousins, also developed epidermoid carcinoma approx. 25 yr. following the appearance of the verruciform lesions.

- 64-2234 ON ENDOMETRIOSIS AND CANCER. (Ger.) Friebe, H.-G. (U. Gynec. Clin., Homburg/Saar, Germany). Zbl. Gynaek. 85(48): 1710-1717, 1963.

A review (46 references) of 94 cases, reported in the literature from 1867 to 1962, of malignant degeneration of endometriosis or adenomyosis and a detailed description of the author's case of a 38-year-old pt. who developed an adenocarcinoma 3 yr. after removal of the uterus and left adnexa because of endometriosis and adenomyosis uteri.

- 64-2235 POSSIBILITY OF MALIGNANT TRANSFORMATION OF CELLS BY ENDOGENOUS NUCLEIC ACIDS. (Hun.) Desbordes, E. (János Hosp., Hungary). Magy. Onkol. 7(2):92-96, 1963.

The author emerges from an examination of current theories of carcinogenesis (28 references) with the conclusion that malignancy is triggered by nucleic acids released in the breakdown of immature cells. Undifferentiated embryonic, reproductive, and reticuloendothelial cells and juvenile granulocytes are incriminated, as are enzyme defects in the organism. Phenomena similar to bacterial transformation, transduction, and conjugation may also account for malignization in higher organisms. Dividing cells in tissue growing near disintegrating tissue or subjected to the action of hormones are regarded as particularly susceptible to such transformation. The release of nucleic acid from disintegrating malignant cells may lead to further cell

transformation and so to the infiltrative propagation of tumors.

- 64-2236 LYPHEDEMA, HYPERPLASIA AND TUMEFACATION OF THE LYMPHATIC TISSUE IN RATS RECEIVING A DIET DEFICIENT IN MAGNESIUM. (Fr.) Jasmin, G. (Dept. Pathol. Anat., U. Montreal, Canada). Rev. Canad. Biol. 22(3-4):383-390, 1963.

Female, Sprague-Dawley rats receiving a magnesium-deficient diet and inj. daily with histidine monohydrochloride (1 mg/day, s.c.), developed anemia; generalized, s.c. edema; accumulation of lymph in the thoracic and peritoneal cavities; hyperplasia of the lymphatic tissue (especially, the thymus); and multiple lymphoblastic nodules of the thymic parenchyma.

- 64-2237 IMMUNITY IN CANCER OF PLANTS. (Fr.) Rybak, B. Rev. Path. Gen. (748): 581-588, 1963.

In a review (14 references) of inherent monocotyledonous and "acquired" dicotyledonous resistance to crown gall induced by infection with *Agrobacterium tumefaciens*, the author concludes that true immunity or immunization is not involved. He states that the phenomenon results from a combination of nitrogen deficiency and relatively high level of tannin content, even though it is associated with the secondary development of an antitumefacient bacteriophage.

- 64-2238 EXPERIMENTAL INDUCTION OF HEPATOMA. HISTOCHEMISTRY. (Fr.) Desmet, V. and J. Vandenbroucke. Lyon Med. 210(48):1144-1145, 1963.

The greater the morphologic difference between a hepatic tumor and the normal hepatic parenchyma, the greater the difficulties seen with respect to glycogen synthesis and metabolism of carbohydrates, G-6-P-ase, and D-G-6-P. In both well and poorly differentiated tumors, characteristic, progressive changes appeared with respect to the distribution and activity of ATP-ase, 5'-nucleotidase and alkaline phosphatase: loss of polarity of localization in the initial stage of tumor development being followed by complete disappearance of the enzymes in a later stage. Loss of polarity of localization of acid phosphatase, in turn, was followed by its dispersion throughout the malignant cell, prior to a marked diminution of both quantity and activity; although acid phosphatase reactions were strongly positive in both macrophages and necrosing tumor cells. Non-specific esterase appeared to be affected in the same way. Leucine-aminopeptidase showed a peribiliary localization in Type I hepatomas, but disappeared entirely in less well differentiated types. The presence of this substance in fibrosing tumor stroma as well as in the fibrous septa

of noncancerous cirrhotic livers suggests that this represents a change of functional state, rather than a precursor of malignant infiltration.

4-2239 SPONTANEOUS TUMORS IN THE SPRAGUE-DAWLEY RAT: INCIDENCE RATES OF SOME TYPES OF NEOPLASMS AS DETERMINED BY SERIAL SECTION VERSUS SINGLE SECTION TECHNIQS. (E.) Thompson, S. W. (Fitzsimons Gen. Hosp., Denver, Colo.) and R. D. Hunt. Ann. N.Y. Acad. Sci. 108(Art. 3):832-845, 1963.

Histopathologic studies of tissue sections from various organs of Sprague-Dawley rats which were fed a 100% γ -irradiated, composite diet and allowed to live out their normal life-spans were made originally by single section technics. Among 177 rats, the number of tumors observed by random single tissue section versus serial tissue section technics were: 9 versus 55 light-microscopic adenomas of the thyroid, 7 versus 11 pheochromocytomas, 5 versus 8 pituitary adenomas, 0 versus 1 papillary adenocarcinoma of the ovary, and 1 versus 6 endometrial polyps of the uterus. None of these additional tumors had been detected by gross examination at necropsy. Although 4 tumors of the brain were observed grossly at necropsy and/or by single sections, no additional tumors were found upon examination of serial sections of the brains of 126 of the rats. No testicular tumors were demonstrated by either method in 45/63 male rats which were studied by both technics.

4-2240 EXPERIMENTAL STUDIES ON DESOXYRIBONUCLEIC ACID PREPARATIONS FROM MOUSE TUMORS. (E.) Divekar, M. V. (Dept. Appl. Biol., Indian Cancer Res. Ctr., Parel, Bombay), N. A. Divekar, S. V. Bhide and K. J. Ranadive. Indian J. Med. Sci. 17(9):734-739, 1963.

When DNA extracted from a spontaneous mammary adenocarcinoma maintained in C3H (Jax) strain mice (DNAC) or a chemically induced fibrosarcoma maintained in Swiss mice (DNAS) was inj. s.c. (100 μ g/wk.) into C3H (Jax) females or, in the case of the first tumor only, into C57BL females for periods of 4, 6 and 8 mo., there were no obvious gross changes in the endocrine organs when compared to controls receiving saline. RNA content of liver, kidney, spleen and ovary of the C3H (Jax) mice treated with DNAS was equivalent to that of controls for up to 6 mo. of treatment but was significantly lower than controls after 8 mo. RNA content of the organs of animals treated with DNAC was not different from controls up to 4 mo. of treatment but increased thereafter. In the case of DNAS treatment, the DNA level of the organs increased slightly after 6 mo. treatment and thereafter showed no significant difference from controls. In C57BL mice treated with DNAC, there was little effect in organ RNA up to 6 mo., following which there was a significant decrease. There was no effect on DNA content.

64-2241 SYMPATHETIC OPHTHALMIA ASSOCIATED WITH MALIGNANT MELANOMA. (E.) Easom, H. A. (2266 N. Prospect Ave., Milwaukee, Wis.). Arch. Ophthalmol. (Chicago) 70(6):786-790, 1963.

In 5/6 cases of malignant melanoma associated with sympathetic uveitis among 400 cases of sympathetic ophthalmia (on file at the Registry of Ophthalmic Pathology, Armed Forces Institute of Pathology, Washington, D. C.), there was unequivocal evidence of a penetrating wound of the eye. In the other case, while there was no evidence of a penetrating wound from study of the few microscope slides available, the history of swelling and diplopia suggested unsuspected trauma. It is concluded that intraocular malignant melanoma has yet to be proved a primary cause of sympathetic ophthalmia. In this uncommon combination, the existence of extraocular extension of the tumor or of a wound of previous penetration is almost a certainty.

64-2242 CLINICAL AND PATHOLOGICAL STUDY OF LIVER CIRRHOSIS AND HEPATOMA IN NAGASAKI DISTRICT. (Jap.) Yokota, M. (Dept. Int. Med., A Bomb Hosp., Nagasaki, Japan), S. Yasuhi, S. Uemura, H. Mukae, G. Matsukuma, S. Otsuru, I. Nakayama, H. Yokouchi, M. Kamido and E. Funakoshi. Nippon Naika Gakukai Zasshi (J. Jap. Soc. Intern. Med.) 52(5):492-493, 1963.

There were 207 cases of liver carcinoma, cirrhosis or combinations of the two among 3,189 autopsies performed in Nagasaki district during 16 yr. The combination was seen in 50.3%, although the figure for the last yr. was 80.8%. This incidence of liver carcinoma + cirrhosis was approx. 2x that of the av. incidence for all of Japan (however, no statement was made regarding possible exposure to the atom bomb). After histological study, it was concluded that liver carcinoma was less frequent in the presence of cirrhosis where the cells showed much damage. The concurrent incidence was higher in the presence of liver cirrhosis with slight or moderate damage to the cells and where there was marked regeneration of cholangioles.

64-2243 A RARE CASE OF SARCOMATOUS DEGENERATION OF A CHELOID. (E.) Biemans, R. G. M. (Dept. Surg., H. Joannes de Deo Hosp., The Hague, The Netherlands). Arch. Chir. Neerl. 15(11):175-185, 1963.

A 27-year-old woman of Malayan-European ancestry, with a lifelong history of tendency to cheloid formation, developed a spontaneous, metastasizing, spindle cell fibrosarcoma from an untreated cheloid on the ventromedial aspect of the thigh. Other cheloids had been treated previously by surgery, X-ray, and inj. of hydrocortisone; and the pt. had been treated systemically, less than a yr. before the appearance of the tumor, by i.m. inj. of Streptotibin (dihydrostreptomycin triisonicotinyl hydrazone pyruvate).

64-2244 LICHEN RUBER PLANUS AND SPINOCELLULAR CARCINOMA. (It.) Depaoli, M. (Inst. Clin. Derm., U. Turin, Italy). Minerva Derm. 38(10):311-317, 1963.

Two cases of lichen rubber planus are described which developed into spindle cell carcinoma after a long period of chronic inflammation and irritation, plus exposure in 1 case (a pt. with hyperkeratotic lichen verrucosus) to protracted arsenic therapy + X-ray. The second pt. had a lichen of the oral mucosa.

64-2245 DISTRIBUTION OF ABO BLOOD GROUPS IN DUODENAL ULCER GASTRIC ULCER AND GASTRIC CARCINOMA IN CAGLIARI PROVINCE. (It.) Pisano, M. (Dept. Gen. Surg., U. Cagliari, Sardinia, Italy), G. Binaghi and G. Boero. Rass. Med. Sarda 65(4):437-447, 1963.

Percentage incidence of blood groups O, A, B and AB among 202 pts. with gastric carcinoma in Cagliari Province was, resp., 50.49, 39.10, 7.42 and 2.97; incidence among normal subjects was 53.91, 32.62, 10.60 and 2.85. The differences were not statistically significant.

64-2246 TRAUMA AND SKIN CANCER. IMPLANTATION OF EPIDERMAL ELEMENTS AS POSSIBLE CAUSE. (E.) Neuman, Z. (Hadassah U. Hosp., Jerusalem, Israel), N. Ben-Hur, and J. Shulman.

Plast. Reconst. Surg. 32(6):649-656, 1963.

Trauma as a possible mechanism of skin cancer is described: postulated as necessary are (1) implantation or displacement of living epithelial elements into the deep subcutaneous area and (2) damage to the subcutis and paralysis of the cellular and enzymatic mechanism which fights against the abortive attempts of epithelial elements to form hair follicles and glands; these attempts may then become wild and develop into skin cancer. Five cases are described in which a single trauma resulted in a verified cancer; in 1 pt. a direct relationship was observed between an epidermal inclusion cyst and basal cell carcinoma, and, in another, cancer in more than one area with healed areas in between.

64-2247 THE ETIOPATHOGENESIS OF CONGENITAL MALIGNANT KERATOMA. (It.) Colla, G. (Clin. Obstet. Gynec., U. Turin, Italy) and L. Pazzaglia. Minerva Derm. 38(11):343-350, 1963.

A woman who had borne a healthy, illegitimate son gave birth to 3 legitimate sons in succession who suffered from congenital malignant keratoma. The father of the 3 keratomatous children had had 2 previous male children, both of whom were healthy. In the established absence of exogenous or endogenous non-genetic factors, the incident appeared to support the role of an hereditary factor in the pathogenesis of this disorder.

ERRATA:

1(5): Subject Index, p. xii, column ii, under Virus, change RP112 to RPL 12.

1(8):#1468, 1963. Line 6, change #1468 to #1467.

1(9-10): 1964. Author Index, p. i, under Irino, S., change 1731 to 1732.

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National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

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